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Original Articles

THE PRESENT STATUS OF THE SURGERY OF SYSTEMIC GOITRE.

—ILLUSTRATIVE CASES.

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DEFINITION.—The term "systemic goitre," which, so far as I am aware, has never been employed by others, seems to me to be the simplest and clearest definition of a clinical picture which is dominated by the exhibition of symptoms due to the introduction into the system of thyroid juices and toxins.

This symptom-complex, commonly known as exophthalmic goitre, Grave's disease, or Basedow's disease, may result from an increased amount of thyroid secretion (hyperthyroidism), or from the altered properties of the secretion (dysthyroidism). The entire organism is affected by the abnormal absorption of thyroid secretion. More or less marked enlargement of the thyroid gland is the usual concomitant of this condition, but this enlargement is not necessarily commensurate with the severity of the systemic symptoms.

Systemic goitre is to be differentiated from simple goitre in which, no matter how great the enlargement of the thyroid gland, there is an entire absence of thyreotoxic symptoms.

CASES AMENABLE TO NON-SURGICAL TREATMENT.

In a certain proportion of cases, when taken early, especially in young women, systemic goitre may be cured, or the patient restored to a fairly normal condition, by rest, topical applications of cold, the use of various sedatives, electricity, or serotherapeutic agents, notably Rogers' serum. It is not, however, the purpose of this communication to discuss the various non-surgical methods which have been suggested and employed in the treatment of this condition.

SYSTEMIC GOITRE A SURGICAL DISEASE.

Despite the fact that some cases yield to medical treatment, pronounced systemic goitre is considered, by consensus of present-day opinion, to be a surgical disease. It is not the intention to tax the reader's time and patience with a resumé of the various surgical procedures which have been tested and discarded.

Experienced modern operators are practically agreed in recommending early radical intervention in the treatment of the vast majority of systemic goitres. The choice of the method, or the modification of the procedure, must be governed by the type and size of the goitre, as well as by a series of other considerations.

It may be stated in passing that certain procedures have been largely discarded because of their perilous nature or imperfect results. Among these may be mentioned interventions on the cervical sympathetic nerve, injections into the gland, and total thyroidectomy.

SURGICAL PROCEDURES.

According to the requirements of the given case, the surgeon has at his disposal the methods of (1) *Partial Thyroidectomy, Strumectomy, Excision or Extirpation*; (2) *Intracapsular Enucleation* (of goitre nodules); (3) *Evacuation or Exenteration* (of goitre nodules); (4) *Resection*; (5) *Vascular Ligation*; (6) *Combined Procedures*.

The interventions which have stood the test of time, and which are now chiefly employed, are partial thyroidectomy and vascular ligation. The other procedures are very briefly considered.

INTRACAPSULAR ENUCLEATION.—Enucleation of the goitre nodules, from the more or less preserved thyroid tissue, according to Socin, is feasible in all encapsulated goitres. Unfortunately, the operation in many cases is impossible without severe hemorrhage. Results with regard to recurrence are as favorable after this procedure as after extirpation of the diseased half of the organ. Paralysis of the inferior laryngeal nerve may be avoided by proper care, and an existing paresis of this nerve has

been known to subside after intraglandular enucleation.

EVACUATION OR EXENTERATION of the goitre



Fig. I.—Case I. Condition before operation. Melancholia apparent in expression.

nodules, a procedure consisting in their incision and the removal of the contents, is very rarely indicated.

RESECTION of the goitre is performed especially in the presence of multiple nodules, or in parenchymatous goitre, when enucleation is not called for.

PARTIAL THYROIDECTOMY OR STRUMECTOMY.—Several methods of goitre extirpation or strumectomy are applicable to the diseased half of the thyroid gland, the other half being either entirely or largely healthy. In the majority of cases partial thyroidectomy is limited to the lobe of the gland which is seriously enlarged, usually the right. When it can be detached without undue difficulty, it is generally ablated in continuity with the extirpated lobe. Almost two-thirds of the goitre may be removed in this manner, without curtailing the thyroid parenchyma. Still more radical resections have their advocates, but there seems to be no real need for such extensive removal of thyroid tissue, as it is always possible, in case of recurrence, to resect the second lobe or to ligate the vessels.

Partial thyroidectomy is often simplified in systemic goitre, as compared with ordinary goitre, by the small volume of the tumor, which is rarely deep seated. However, adhesions with

neighboring structures are very common. The greatest danger consists in the the acute and often fatal disturbances which have been observed to follow immediately upon the operation, even when this is restricted to the very simple manipulations. Death from collapse has been known to occur within a few days or even hours, preceded by extreme tachycardia and violent excitement. Tetanic contractures are not observed, however, unless the operation has been very extensive. The pathogenesis of these symptoms has been referred either to a hyperacute thyroid intoxication, in the course of the work upon the gland (thyreotoxic theory); or to a hyper-stimulation of the vasomotor and trophic nerves of the region (nervous theory).

Bérard pointed out that the first of these theories seems to be more correct, in view of the fact that the same disturbances in modified form have been known to follow in goitre cases after the thorough brushing and scrubbing of the cervical region in preparation for operation. This thyroid massage, according to Bérard, suffices for a toxic discharge into the circulation. The accuracy of this observation has been questioned by Berry, whose large experience with these cases does not confirm the efficiency of



Fig. II.—Case I. One month after operation.

rough manipulation of the gland in the production of toxic symptoms.

Provided total extirpation is avoided in stru-

mectomy, and a sufficient portion of the thyroid gland is left behind, cachexia strumipriva, a condition due to the entire loss of the organ, is not observed to follow. Provided the part which has been left behind is capable of functioning, one-fourth of the gland, or one-half of one-half of the thyroid, seems to be entirely sufficient in this respect.

Garré was enabled to re-examine over twenty of his systemic goitre cases which had been operated upon more than five years previously, almost invariably by hemilateral extirpation. There were eighty-five per cent. of recoveries, with many great improvements, and sixteen per cent. of absolute cures. No improvement was noted in fifteen per cent., including three per cent. of deaths. One patient with an enlarged thymus died on the table under general anesthesia with ether. In contradistinction to the above results of surgical treatment, the mortality percentage of medical treatment amounted to twelve per cent. in moderately severe cases, reaching twenty-three per cent. in grave cases.

In the opinion of Kausch, bilateral wedge-shaped excision of the goitre, according to Mikulicz, is preferable to unilateral extirpation (Kocher's operation), mostly on account of the better safeguarding of the recurrent laryngeal nerve and the parathyroids. With special re-

moving such portions of the thyroid gland as seemed advisable, without paying any attention whatever to the parathyroids."



Fig. IV.—Case II. Three weeks after operation.



Fig. III.—Case II. Before operation, showing goitre.

ference to the latter, it is noteworthy that Berry, who regards the parathyroid teaching as a myth, has been for many years "in the habit of re-

As a preliminary step in partial thyroidectomy removal of the thymus gland is recommended by some surgeons. A close relationship between systemic goitre and the affections of the lymphatic system, known as pseudoleukemia and Mikulicz's disease, seems indicated by some of the modern investigations. This connection is suggested by certain histological changes in these goitres, and by the demonstration of a persistent thymus in about ninety per cent. of all operations for systemic goitre. Aside from confirmatory findings in experimental investigation, such a connection is indicated by the operative results obtained by Coenen, who secured marked improvement in a case of systemic goitre through the removal of the persistent thymus gland. Spijarny, who holds that a persistent thymus is found in eighty-two per cent. of the deaths from systemic goitre, considers this a contraindication to the operation. In patients who die after goitre operations, persistency of the thymus is noted in a very high percentage of cases.

There is thus a tendency to credit a persistent thymus with a considerable part in the pathogenesis of systemic goitre. It is important, therefore, that this factor be borne in mind in the treatment of the disease.

VASCULAR LIGATION.

Ligation of the superior and inferior thyroid arteries, on one or both sides, in one or several sessions, has been recommended in order to induce atrophy of the goitre, especially in the rapidly growing parenchymatous goitres of youthful individuals, or in cases of systemic goitre. Ligation is also used as a preliminary operation with the hope of improving the condition enough to allow a more radical operation at a later time. Kocher never ligates more than three thyroid arteries, on account of the danger of cachexia when the four arterial vessels are obliterated. The method of ligating several arteries in these cases was considered by its originator, Mikulicz, as a more difficult and dangerous operation than thyroidectomy. Aside from the danger of the intervention itself, the thyroid arteries must be tied at the same time, to insure maximum efficiency; for, instead of being terminal vessels, these arteries freely communicate through anastomosis between themselves, and through collateral circulation with the arteries of the vicinity.

In severe cases of systemic goitre, successive ligation of first one and then another artery

Berry's observations, the inferior is nearly always a much larger vessel than the superior thyroid. Ligation of the inferior thyroid is a

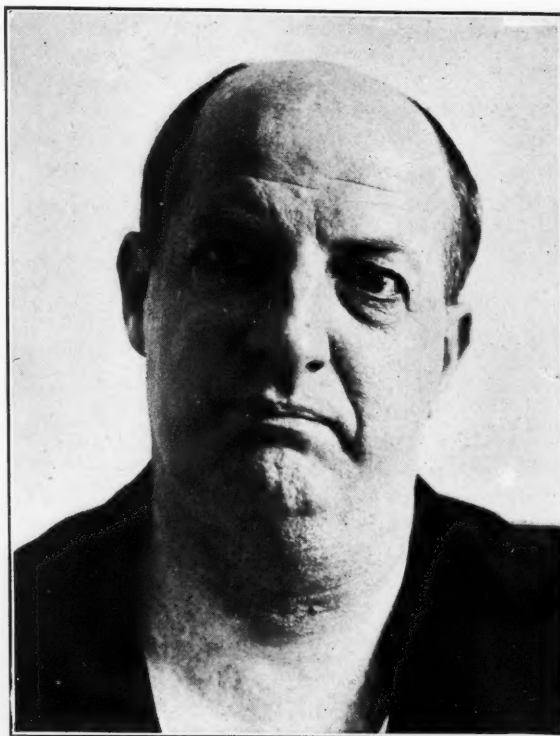


Fig. VI.—Case III. Before operation.



Fig. V.—Case II. One and a half years after operation.

may be applied under local anesthesia. Being more accessible, and not related to any important nerves, the superior thyroid arteries are usually selected for the ligation. According to

very difficult and rather severe procedure, which should be reserved for special cases. The place of selection for the ligature is directly internal to the point where the thyroid artery crosses the common carotid. The ligature is applied flush with the carotid, at a distance from the gland, and therefore from the recurrent nerve. The chief difficulty is referable to the chronic inflammation of the tissues surrounding the goitre.

Ligation of one or more arteries acts, in the opinion of Bérard, not only by cutting off the nutritional supply of the gland, but undoubtedly also by affecting the metabolism through the exposure, sketching, and tying of the concomitant nerves of the vessels. The goitre is rarely large enough to interfere with the exposure of the arteries.

Successive ligatures were applied by Kocher in order to avoid all danger of myxedema. In 1895 he published thirty-four observations with thirty-one cures or improvements, and three deaths (one not due to the operation). At the German Surgical Congress in 1895, Rydygier compared his results with those of Kocher. By the ligation of the four arteries in a single session he obtained among twenty-two cases, twenty cures or improvements. There were two failures, without any serious complication, tetany or myxedema. In the experience of

Weinlechner, tetany has been known to follow upon the ligation of the two superior thyroid arteries.

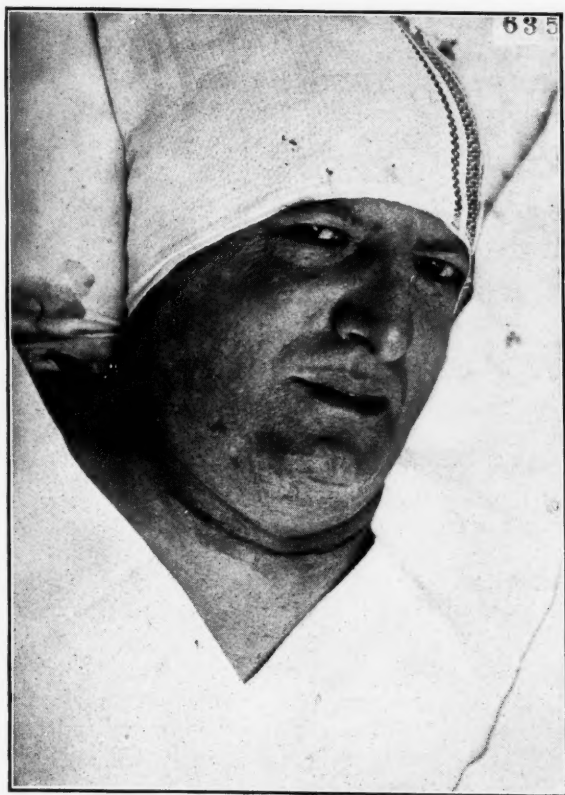


Fig. VII.—Case III. Immediately after operation. Wound sutured, ready for dressing.

Bilateral ligation of the inferior thyroid arteries, with resection of the right sympathetic nerve, was performed by Patel and Leriche, in the case of a woman twenty-six years of age. The large goitre diminished in size, but soon increased again, and six weeks later the right half of the thyroid was extirpated. The patient rapidly succumbed to cachexia, within three weeks of the operation, and at autopsy a thymus gland the size of a walnut was found, although clinically the case was not one of thymus death. The mortality of vascular ligation, both single and double, in the worst types of the disease, in Mayo's experience fully equalled or exceeded the mortality of thyroidectomy.

According to Mayo, the method of ligation now has an accredited position in the treatment of systemic goitre. He states that patients seen in the early stages are sometimes wonderfully improved by the simple operation of double ligation. In mild cases, or when the patient is operated upon at an early date, ligation of the blood and lymph vessels is recommended by him in the treatment of hyperthyroidism. This intervention serves to prevent the production as well as the outpouring of the secretion, and a complete cure frequently follows.

The same is adopted by a number of operators

in the very grave cases, which are thereby essentially improved, so that the larger lobe with the isthmus can be removed later under more favorable conditions. The general health is often greatly benefited by the ligation, and the patients gain in weight.

SELECTION OF OPERATIVE METHOD.

The unilateral type of systemic goitre always affords favorable prospects for operative interference. In a general way, after the patient has been prepared by improving the general condition, three-fifths of the goitre may be removed.

Kocher, in a recent contribution, emphasizes that operative procedures are not only permissible, but positively indicated in all goitre cases where an increased function of the thyroid gland can be demonstrated by clinical observation and examination of the blood. Two or three of the main arteries may be tied, first on one side, then on both sides. In case the result is not sufficient, a portion of the goitre may be extirpated in the third session. One-half of the gland or the more considerably enlarged lateral lobe, may be removed, practically always with the certainty that not too much has been ablated, and without risking the onset of symp-

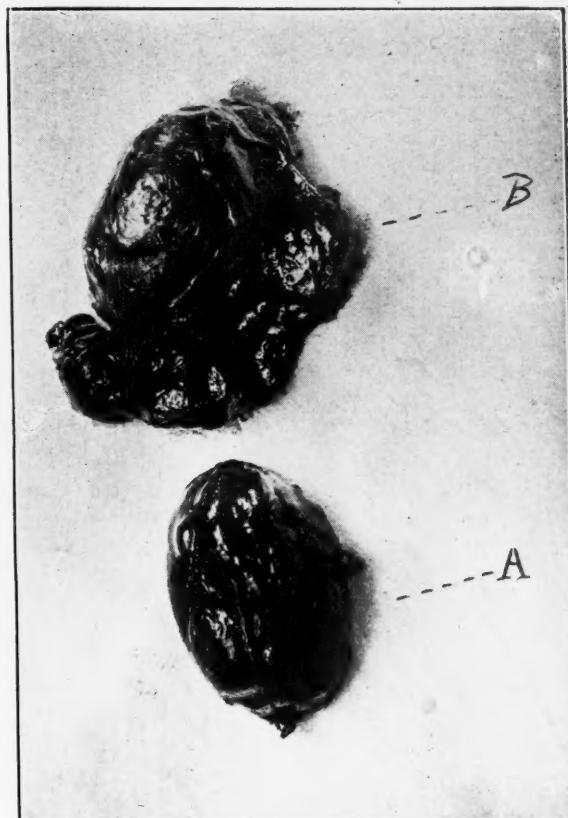


Fig. VIII.—Case III. A. left lobe of thyroid. B. growth from isthmus—mediastinal goitre.

toms due to loss of thyroid function.

Vascular ligation and partial thyroidectomy have been combined in such a way that uni-

lateral excision is performed with ligation of an artery of the opposite side. This procedure is advocated by Landstroemme. In recurrent



Fig. IX.—Case IV. Before operation.

goitres an attempt may be made to induce atrophy of the remaining lobe through application of a ligature around one or both of the remaining arteries. If the reaction after the ligation of the vessels at the left upper pole be not severe, the right lobe, the isthmus, and possibly a portion of the left lobe, are removed by Mayo at a second operation.

In thirty-two cases of systemic goitre, cured by operation, reported by Klemm in 1908, the intervention always consisted in excision of the diseased half of the gland. Where the entire gland was affected, the excision was combined with ligation of the vessels of the opposite side. The operation was invariably performed in one session, under local anesthesia.

As a surgical curiosity, the anastomosis of the central end of a thyroid artery with the peripheral end of a thyroid vein has been suggested, in selected patients, with the object of diminishing the goitre without a strumectomy. Although the operation is hardly easier than strumectomy, it is claimed to offer the advantage of better avoidance of operative complications, especially injury to the recurrent nerve.

OPERATIVE RESULTS.

In eleven cases of systemic goitre reported by Krueger in 1908, vascular ligatures were ap-

plied, under general anesthesia, in three instances, with one death. Partial strumectomy was performed in the eight remaining cases, always with radical improvement.

Mayo's goitre operations exceed two thousand in number, and contain series of seventy-six to ninety cases without a death. About seventy per cent. of the patients consider themselves as entirely cured. In a recent contribution (1912) he reported having operated on a consecutive series of 278 cases of exophthalmic goitre without a death.

Early interventions upon ordinary goitres have so low a mortality as to render this danger practically negligible at the hands of skilled operators. In case of the combined procedures, as well as in simple strumectomies, the operative mortality has been extraordinarily diminished of recent years. Jaboulay has not lost a patient operated upon for benign goitre since 1900; and Bérard operated with the same success on a series of eighty-five cases between 1900 and 1908. Kocher's record of his fifth thousand of goitre operations in the Bern Clinic, completed on March 11, 1912, stands as follows: Among 603 uncomplicated, although in part very difficult goitres, there was no death due to the operation. The same remark applies to nineteen operations for recurrent goitres, which are apt to prove especially difficult on



Fig. X.—Case IV. One year later.

account of cicatrices or adhesions. Of 26 excisions in malignant goitre, all patients were cured. Thyroid operations, when properly per-

formed, lead usually to a cure or at least to an improvement of systemic goitre, in the experience of Kocher. Definite end-results could be compiled in 320 operative cases, recently reported by this authority (1912). A complete cure was obtained in 150 of these patients, while 148 still present individual symptoms of the disease, such as protuberant eyes or functional disturbances of thyroid origin, but with marked general improvement. The outcome was unsatisfactory in only 22 cases, either because the operation could not be completed, or on account of recurrence, in five per cent. of the cases; or because secondary disturbances on the part of the kidneys or the liver failed to subside after the goitre operation.

Concerning permanent results of operative treatment of systemic goitre, Weispenning (1912), writing from the First Surgical Department of the Hamburg-Eppendorf General Hospital, Service of Professor Kümmell, points out that the cases operated upon during 1889 to 1900 have already been re-examined twice, first by Schulz, in 1911; then by Friedheim, in 1905. The re-examination of Schulz covered twenty cases, the longest interval since the operation being eleven years, the shortest one and one-quarter years. In eighteen of these twenty cases, the operation proved to have been

Friedheim, nearly five years later, showing permanent cures in fourteen cases; marked improvement in two cases; and moderate improve-



Fig. XII.—Case V. One month after operation.



Fig. XI.—Case V. Before operation.

perfectly successful; of the remaining two cases there was one failure and one death. The nineteen survivors were again examined by

ment in three cases. The fourteen cures must be considered permanent, as, in the last case operated upon, four years had elapsed at the time of the re-examination. Of these nineteen cases, five were examined for the *third* time by Weispenning, who also carried out the first re-examination in eleven of fifteen cases operated upon from 1900 to the beginning of 1910. The sixteen re-examined cases are divided by him into four groups, according to results:

- (1) Permanent cures, four cases.
- (2) Temporary cures, three cases.
- (3) Improvements, two cases.
- (4) (a) Recurrences, five cases.

(b) Cases with goitre of the side not operated upon, two cases.

In thirty-five operative cases, the findings in 1911 were:

Permanent cures, fifteen cases, forty-three per cent.

Temporary cures, three cases, eight per cent.

Improvements, two cases, seven per cent.

Recurrences, seven cases, twenty per cent.

Deaths, three cases, eight per cent.

Not re-examined, five cases, eight per cent.

The operation in all cases had an immediate beneficial result. In some this became permanent. In others it proved transitory, either because of a recurrence, or of the subsequent development into a goitre of the part of the

thyroid which had been left behind. In the latter event the hyperthyroidism which the operation had temporarily relieved returned

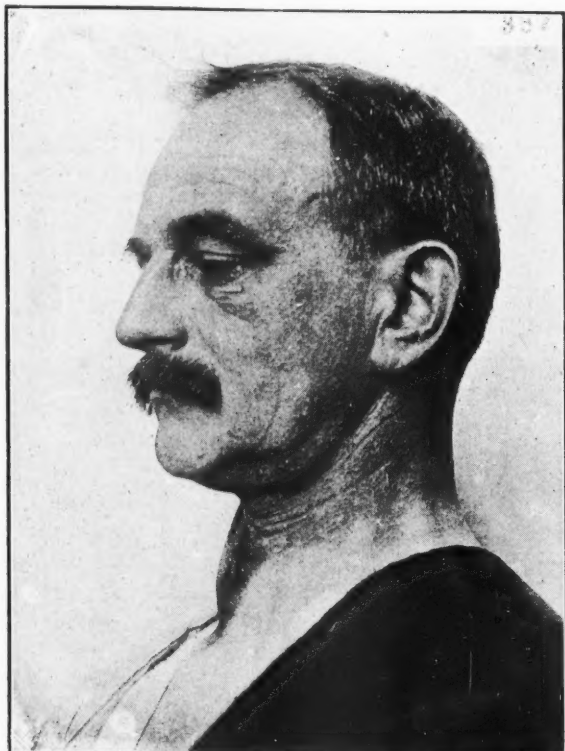


Fig. XIII.—Case VI. Condition before operation.

sooner or later after the interference, eliciting in part or entirely the typical objective and subjective symptoms of the disease. This outcome of operative intervention again corroborates the belief of Kocher, Kümmell, Mayo, and other experienced operators, in the efficiency of surgical procedures in systemic goitre, the operation to be performed at the earliest possible moment, while the disease is still in its incipency.

In the Mayo clinics, during the years, 1905, 1906 and 1907, two hundred operations were performed for hyperthyroidism. Of this number, twenty-two were males and one hundred and seventy-eight females. Ten patients died as the result of the operation. Letters were sent to the remaining one hundred and ninety and answers were received from one hundred and sixty-seven. Of these, one hundred and sixteen, or 70 per cent., were cured; thirty-two, or 19 per cent., improved; ten, or 5.8 per cent., slightly improved; nine, or 5.2 per cent., not improved.

Klose's compiled statistical material from several large clinics with altogether two hundred and ninety-eight cases (1911) shows:

191 cases, sixty-four per cent. cures. (Two to eighteen years).

72 cases, twenty-four per cent. improvements.

7 cases, three per cent. not cured.

6 cases, two per cent. recurrences.

22 cases, seven per cent. deaths.

Concerning the functional results after the various operative procedures, the dyspnea and dysphagia which most frequently require intervention, are amenable to improvement, provided these symptoms are due to the goitrous enlargement itself. Nearly asphyxiated patients not uncommonly regain free and easy respiration on the day of the operation, and such favorable results are noted in about three-fourths of the cases. Difficulty in swallowing is apt to persist and even increase during the first week following the operation, after which time it gradually subsides.

As soon as the operation has stopped the hypersecretion of the thyroid gland and removed the obstruction of the return circulation, there is usually an end of the cardiovascular disturbances, such as tachycardia, palpitation or persistent edema of an upper extremity. The results are not so positive when the structure of the myocardium has been affected, although even in these cases there is often a striking improvement. Together with the regulation of the heart action and the subsidence of the chronic pulmonary congestion, the functions of the other organs are also improved, in consequence of the better blood supply. Aside from exception-



Fig. XIV.—Case VI. Operation complete. Wound sutured, ready for dressing.

ally unfortunate cases, in which myxedema follows even on limited resections, the signs of thyroid insufficiency gradually subside, the re-

maining lobules of the gland assuming increased activity.

With special reference to nervous disturbances, the recurrent nerves, being in closest contact with the goitre, are apt to be profoundly altered by it. In some cases, where the muscles of the larynx had not become entirely atrophied, the removal of the thyroid swelling has been known to relieve even total laryngoplegia. In several observations of Roux and of the author, the patient's hoarse and goitrous voice became perfectly normal after the operation. Bérard noted two cases in which the ablation of the goitre relieved neuralgic disturbances of the upper extremity, with incipient atrophy of the muscles of the shoulder.

The cases of improvement after operative treatment, according to Friedheim, illustrate the importance of correct dosage of the part of the goitre that is left behind. In some of his cases, a goitre was again present at the time of the report, so that a cure was still to be expected from a second or third operation. His investigations were made upon a series of twenty cases of systemic goitre, from the clinics of Kümmell, which were treated by enucleation or resection of a portion of the goitre. Later reports could be secured from sixteen of these patients. Fourteen were found to be cured, no trace of the goitre being left. There were two marked improvements, three moderate improve-

of from four to fifteen years after operation.

In reporting the results of surgical treatment in systemic goitre before the French Surgical



Fig. XVI.—Case VII. Before operation.

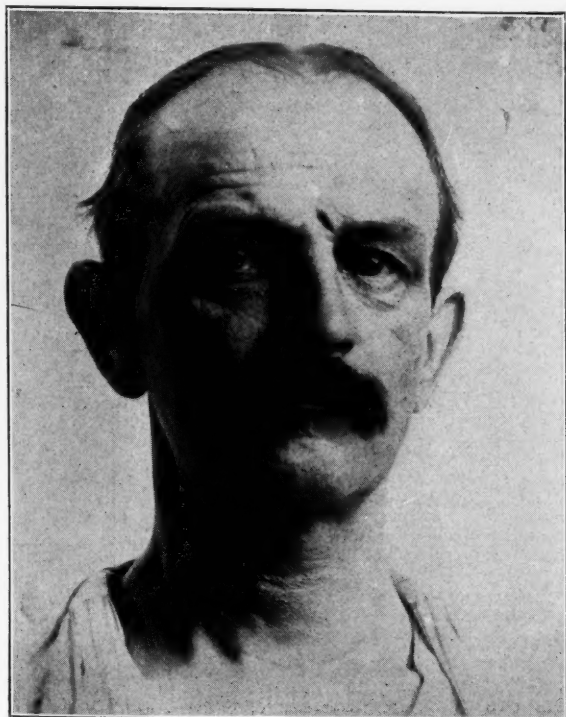


Fig. XV.—Case VI. Two months and a half after operation.

ments, and one death due to tetany, ten days after the operation. At the time of the report the fourteen permanent cures covered periods

Congress, in 1910, Delore and Lenormand state the following figures: Internal treatment yields twenty to twenty-five per cent. cures, ten to twenty-five per cent. mortality. Surgical treatment of the thyroid itself has a mortality of from zero to seven per cent., average four per cent., as calculated for about fifteen hundred operations. Cures, seventy-five per cent., according to Kocher; fifteen per cent., according to Garré. Including the great improvements with the cures, there are six hundred and sixty-six favorable cases, as compared to one hundred and seventy-four slightly improved or recent cases, and sixty-three deaths due to operation. Since the publication of this report, the operative morality has been strikingly diminished.

SUMMARY.

It may be said that the internal or medical treatment of goitre and other affections of the thyroid gland has failed to show results even approaching those realized by the handiwork of the surgeon. The organo- and serotherapeutic results are often of only limited duration, and even in the most favorable cases frequently require periodical repetitions of the treatment, for the maintenance of the improvement. Per-

manent cures in the grave forms of the disease are very rare. On the other hand, with modern methods of technic and the proper care before



Fig. XVII.—Case VII. Three and a half years afterwards.

and after operation, the surgical mortality is exceedingly small, while a more or less prompt or progressive improvement, approaching a cure in the majority of cases, is usually obtained by modern goitre operations.

ILLUSTRATIVE CASES.

The following brief histories, with pictures, selected from a large number of cases operated upon by different methods, according to requirements, illustrate some types of operative technic and results. Elsewhere I have dealt with other phases of the subject. (See bibliography).

CASE I.—G. female, aged 55.

Symptoms.—Gradually growing worse for some years. Nervous, rapid heart, tremor, general weakness; enlarged and throbbing neck. At times so depressed as to appear to be a typical case of melancholia.

Operation. July, 1912. Partial thyroidectomy, right half, and a small portion of left upper pole removed, under local anesthesia. Recovery uneventful. Gradual gain in nervous and physical strength. All melancholia disappeared. Perfectly well February 14, 1914.

CASE II.—W., female, aged 68. Referred by Dr. James A. Babbitt, of Philadelphia.

Symptoms.—Slight goitre at 17, which disappeared. Three years ago neck gradually grew larger, until there was absolute loss of voice; marked cyanosis at times; frequency of heart action; nervousness; some tremor.

Operation. August, 1912, under local anesthesia. Removal of right lobe and isthmus. A part of the goitre was markedly calcareous. Recovery uneventful. Within a few days voice began to return. Perfectly well, February 14, 1914. Voice normal, no cyanosis. Practically all symptoms relieved.

CASE III.—G., male, aged 48.

Symptoms.—Markedly nervous; rapid heart; at times extreme dyspnea, with cyanosis; unable to walk upstairs. Getting steadily worse for some months, unable to work, practically an invalid. Definite hyperthyroidism, but also marked local symptoms from displacement of the trachea one and one-half inches to the right, and softening of several of the tracheal rings by pressure.

Operation. February, 1913, under local anesthesia. General anesthesia absolutely contraindicated. Left lobe of thyroid, (Fig. VIII-A), and a growth from the isthmus, (Fig. VIII-B), more than twice the size of the enlarged lobe, removed. Uneventful recovery. Back at work. Well.

CASE IV.—C., female, aged about 48. Referred by Dr. W. H. Cantle, of Mamaroneck, N. Y.

Symptoms.—Nervousness and tremor.

Operation. November, 1912, under local anesthesia. Enormous bilateral goitre, with colloid and cystic degeneration. Inflammation involving the skin. Partial thyroidectomy on each side, including the isthmus, which was markedly degenerated. It was possible to leave a small portion of lower pole of each lateral lobe. Recovery uneventful. Perfectly well February 1, 1914.



Fig. XVIII.—Case VIII. Before operation.

CASE V.—B., female, aged 25.

Symptoms.—Difficulty in swallowing. Enlargement of neck for several years. Nervousness, palpitation, throbbing in neck.

Operation. December, 1913, under oil-ether rectal

anesthesia. Right lobe removed. A preliminary of $\frac{1}{8}$ gr. morphin, $\frac{1}{150}$ gr. atropin, one-half hour before operation. Six ounces of a seventy-five per cent. solution of ether in oil, administered by Gwathmey's method. Anesthesia entirely satisfactory in



Fig. XIX.—Case VIII. One month later.

fifteen minutes. Recovery uneventful. Considers herself well.

CASE VI.—W., male, aged 47.

Symptoms.—For some years had had persistent cough, with sensation of choking. Was advised by family physician to go south for what was diagnosed as early pulmonary tuberculosis. Five weeks before consulting me a small swelling was discovered in the lower part of the neck, right side, which the physician pronounced a tuberculous gland. Upon examination a very small goitre was found. Slight hyperthyroidism, but marked general depletion from constant coughing and anxiety over his supposed tuberculosis condition.

Operation, February, 1912, under local anesthesia. Small goitre, right lobe, lower pole, removed. This enlargement was so situated as to be far down, easily escaping detection. It rested directly upon the recurrent laryngeal nerve. Recovery uneventful. Cough ceased after operation. Perfectly well, February 1, 1914.

CASE VII.—R., female aged 20.

Symptoms.—Had had goitre symptoms for thirteen years. Marked nervousness; tremor; exophthalmos so great that eyelids could hardly be made to cover the eyeballs; pulse between 130 and 150; unable to do any work; practically an invalid.

Operation, July, 1910, under local anesthesia. Complete removal of right lobe, and upper part of left lobe. Recovery uneventful. Perfectly well, Febru-

ary 1, 1914. At work as professional singer and dancer.

CASE VIII.—W., female, aged 52.

Symptoms.—Swelling in neck for twenty-three years, but so slight could hardly be detected. Headache for ten years. At times distinctly short of breath, choking sensation, palpitation, cyanosis, nervousness, eyes abnormally protuberant. Distinct picture of hyperthyroidism, with hardly perceptible goitre.

Operation, April 1913, under local anesthesia. Mass in right lobe enucleated. Ligation of superior thyroid, left side. Recovery uneventful. Perfectly well, February 1, 1914.

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THE ETIOLOGY AND PATHOLOGY OF LOBAR PNEUMONIA.*

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The inflammatory process resulting from the direct action of bacteria upon the lung is called "pneumonia," therefore, pneumonia is an infection of the lungs. Almost all the known pathogenic bacteria have been proved to be capable of producing such infection. To stir up the process it is necessary for the bacteria to invade the lung tissue, and invasion of the lung may occur through the bronchi (inhalation pneumonia) or through the blood and lymph stream (hematogenic or lymphogenic) pneumonia. It is stated¹, however, that bacteria may pass by way of the lymphatics through the lungs without inciting the sequence of events due to their presence. Therefore, whether or not pneumonia is produced must depend upon other factors, such as increased virulence of the bacteria, or decreased resistance on the part of the host, or both. That decreased resistance or increased susceptibility to pneumococcic infections is a factor of the utmost importance will be brought out later.

Pneumonia is today one of the great problems of preventive medicine. Cohen² has recently emphasized the striking fact that the number of cases reported is steadily rising, and that all over the world the percentage mortality in pneumonia is increasing. Until recently this mortality was given as 20 to 30 per cent., but statistics show that it now ranges from 30 to 40 per cent. Such a contrast, considered with the significant fact that the incidence of pneumonia is now greater, in other words, that more cases of pneumonia are occurring every year and that of these cases about ten per cent. more are dying now than a decade or two ago, illustrates quite forcibly the seriousness of this great problem.

Lobar pneumonia is an acute infection caused most commonly by the pneumococcus. This is a somewhat elliptical, lance-shaped coccus, usually found in pairs and definitely encapsulated. It is normally found in the mouth and respiratory passages of healthy individuals, some observers giving a proportion of one out of every three persons, others giving figures as high as 80 to 90 per cent. of positive findings of all cases investigated. Some persons always harbor a virulent type. The virulence of the organism is, obviously, extremely variable. Its viability is not great. When exposed to sunlight it dies within one and one-half hours. In moist sputum in a dark room it may live ten days.

Various other bacteria, such as the pneumobacillus, streptococcus, and staphylococcus may be associated with the pneumococcus in lobar pneumonia, but these are of importance merely as secondary invaders.

Much has recently been added to our knowledge of pneumonia by the notable work of Cole³ and Dochez⁴ on the classification of pneumococci. These investigators have shown that while it is true that a large majority of the cases of lobar pneumonia are due to the pneumococcus, so far as biologic reactions are concerned these cases of pneumococcus pneumonia are caused by at least four different types of organisms. In other words, pneumococci isolated from cases of lobar pneumonia belong to one of four distinct types, each of which manifests specific immune reactions. Because of the inconstancy in differences of morphologic and cultural characteristics of variant strains of pneumococci, and since immunologic reactions manifest a peculiar strict specificity, the latter have been adopted as a basis of differentiation. It was found by protection experiments that the immunization of animals is strictly limited to the particular type of pneumococcus used in the process of immunization, so that by observing the sequence of events induced by injecting into animals virulent cultures of the isolated pneumococcus mixed with protective serums obtained from animals immunized against single varieties, the type of the organism tested can be detected. If this organism belongs to the same group as that from which the serum had been derived the animal is protected from its pathogenic effect, whereas if it belongs to a different group the animal is not protected. It was found, further, that agglutination reactions correspond with these protection reactions. In that way it has been possible to distinguish four distinct groups of pneumococci, known as group 1, group 2, group 3 (mucosus), and group 4 (heterogenous). The first two are made up of organisms closely related immunologically to the others of their respective groups. Group 3 consists of pneumococcus or streptococcus mucosus. Whether or not differences exist between individual members of this group is not yet fully known. Group 4 embraces a number of distinct members which manifest all the cultural and common characters of pneumococci, but do not seem to be related to each other so far as can be demonstrated by specific biologic reactions. Because of the lack of such distinctive common characters these are classed as heterogenous. They were obtained in about 22 per cent. of the cases thus far studied. Almost one-half of the cases studied were due to pneumococci belonging to group 1. The most virulent

*Read at the 40th semi-annual meeting of the Northern Tri-State Medical Assn., Kalamazoo, Mich., Jan. 13, 1914.

1. Principles of Path: Adami and Nicholls, 1909, II, 295.

2. Cohen, S. Solis: Jour. A.M.A., 1913, LXI, 107.

3. Cole, Rufus: *idem*, 663.

4. Dochez, A. R., and Gillespie, L. P.: *idem*, 727.

are those of groups 1 and 2, the least virulent are those of group 4. The direct practical importance of these studies is very evident. Unless the curative serum or vaccine employed in any case is homologous with the pneumococcus causing the infection, it will have no therapeutic value; if, on the other hand, it is homologous, its therapeutic value may be very great.

ETIOLOGY.

As to the etiology of pneumococcic infections, there are many factors of considerable importance. Some of these may now be briefly considered. In general it is said that the predisposition to pneumonia is rather marked up to the sixth year, that it then diminishes up to the fifteenth year, and after that increases with each subsequent decade. The mortality after 65 is more than seven times greater than the period between fifteen to forty-five, and about three times as great as in the period between forty-five and sixty-five years. It is observed in males oftener than in females. No other acute disease recurs in the same individual with such frequency. It is apt to follow as a result of bodily injury, especially when the chest has been injured. It is more fatal in the colored than in the white race. It is more common in the big industrial centers, especially in the overcrowded portions. Those who are exposed to hardship and to cold are particularly susceptible. The highest incidence of pneumonia is in the winter and spring months, more so during the months of February and March. Climate does not really matter very much, as the disease prevails equally in hot and cold latitudes. Moreover, any debilitating condition leading to a lessened vitality on the part of the individual, such as alcoholism, diabetes, Bright's Disease, chronic organic nervous disorders, wasting diseases, exhausting occupations, pulmonary lesions, and so on, are very significant as predisposing or contributory causes.

PATHOLOGY.

In lobar pneumonia the specific anatomic changes occur in the lungs. Part or all of a lobe or an entire lung may be involved, and the process may be unilateral or bilateral. The tendency is for a whole lobe, and the right lower lobe most frequently, to become involved. The inflammation occurs in about 52 per cent. of the cases on the right side, 33 per cent on the left, and in about 15 per cent. on both sides. For the purpose of description four successive stages of the inflammatory process are said to occur. These are (1) stage of engorgement, (2) stage of red and (3) of gray hepatization, and (4) resolution. Such a division is useful only for descriptive purposes, for in this, as in other conditions, the sequence of events is not always typical. Quite frequently several

stages are seen simultaneously at autopsy in the lung. The inflammatory process generally begins with congestion, and is promptly followed by consolidation. In the first stage the pathological condition is one of active inflammatory hyperemia. The lung is redder than normal and rather edematous. Microscopically, the vessels are congested, the epithelial cells are swollen and desquamated, and occasional red blood cells may be found in the alveoli. In the second stage the lung is quite red, swollen, heavier and firmer than normal, it pits on pressure, and is rather friable. On section much blood-stained, turbid fluid can be squeezed out. The exudate contains mostly red corpuscles and some leucocytes. Microscopically, the capillaries are markedly congested, the epithelial cells are swollen, and there is considerable desquamation with filling of the alveolar spaces by these desquamated so-called "catarrhal" cells, red corpuscles, and leucocytes, all enmeshed in a fibrin network. Because of its solidity, its reddish color, and its general appearance, the lung may resemble the liver, hence the term "red hepatization." The first two stages are rarely seen at autopsy, except in individuals dying by accident or in limited areas at the edge of a creeping pneumonia, for nearly all fatal cases of pneumonia are farther advanced in the course of the disease. The next or third stage is that of gray hepatization. The lung becomes more swollen, it is very firm and heavy. The pleura becomes granular-looking and is covered with a varying amount of fibrinous exudate, for in every case of lobar pneumonia there is, in fact, also an associated pleurisy. The lung is friable, non-crepitant, and does not float on water. On section its surface is granular, and of a color varying from reddish-gray to grayish-yellow. Microscopically, the capillaries seem to be obliterated, the alveoli are filled with a purulent exudate and their walls are compressed. The exudate is made up almost entirely of leucocytes with fibrin, occasional red cells and "catarrhal" cells. The final stage of the inflammatory process, or resolution, sets in with breaking up of the fibrin and autolysis of the pus cells. The lung shrinks, and feels boggy. On section it is moist, and of a color ranging from grayish to yellow. Microscopically, the picture is like that seen in the third stage, except that the capillaries are now becoming permeable, and degenerative changes of the fibrin and pus cells have begun. The broken-down exudate is removed chiefly by the lymphatics and to some extent by the expectoration.

Associated with these specific anatomic changes, there is a bacteremia and a toxemia of varying intensity. The pneumococcus can be isolated from the blood in many cases. Prochaska obtained it in all of his 40 cases; Pearce in 97

per cent. of the 125 cases he reported; Rosenow in 91 per cent. of his 145 cases; Kinsey in 75 per cent. of his 25 cases; Hastings and Boehm⁵ in only 30 per cent. of 33 cases they recently reported. In nearly all typical cases there is a definite leucocytosis with an increase in the percentage of polynuclear neutrophilic leucocytes. This appears early, persists, and disappears with the crisis. The degree of leucocytosis is not so much an indication of the extent of pulmonary involvement or severity of the disease as an index of the degree of natural resistance or reaction of the body against the infection. There occurs also a marked retention of chlorides, and this feature is so constant that it is of considerable value in the differential diagnosis of lobar pneumonia.

Attempts have been repeatedly made to learn something about the nature of the general biologic changes that occur within the body and the factors that contribute to the final outcome in lobar pneumonia. As already indicated, most cases recover, and recovery is usually by crisis. In the less fortunate cases the disease may terminate in induration of the lung, the so-called delayed resolution or chronic pneumonia, or in abscess or gangrene of the lung, or in death. Unless some serious accidental complication develops, death is usually due to the development of a general septicemia. The role played by the chemical change of the blood in the causation of death has been discovered quite recently by Peabody⁶. His studies show that in most cases of uncomplicated lobar pneumonia the decrease of respiratory surface is completely compensated for, so that the oxygen content of the blood is within normal limits. It should be emphasized here that so far as the respiratory function itself is concerned, it can be carried on with the lung capacity reduced to a rather small volume, as low as one-sixth according to the recent investigation of Bernard and Mantoux⁷. In the terminal stage of fatal cases of pneumonia where death does not occur suddenly, Peabody showed that there is often a prolonged diminution in the oxygen content of the blood, and with this a progressive decrease in the oxygen—combining power of the blood, probably due to a change of the oxyhemoglobin to methemoglobin. This change in the hemoglobin molecule making it no longer capable of readily taking up and giving off oxygen is probably a factor in the immediate cause of death in many cases.

Many attempts have also been made to gain some knowledge of the nature and sequence of events producing the crisis. Clough's⁸ recent

contribution contains a fund of valuable information on this question. It is now agreed that crisis is brought about by an increase in some of the defensive forces of the body which inhibit the unrestricted development of the bacteria. Clinically it has been found that in favorable cases of pneumonia the percentage of positive blood cultures and the number of organisms present in the blood diminish as crisis is approached. Crisis, then, is coincident with the development of an immunity dependent upon the appearance of antibodies in the circulation. The accumulated evidence shows that there are developed in the blood serum active substances called "bacteriotropines" which bring about active phagocytosis of the pneumococci. Their action is strictly specific, i. e. the phagocytic activity which these bacteriotropines cause is strictly limited to the homologous strain of pneumococci which stimulate their formation, and they differ from the so-called "opsonins" with respect to some of their physical properties. The phagocytic activity of serum containing these substances has been found to run closely parallel with its protective power for animals, so that it is assumed that the protective action of the serum is dependent upon its power of promoting phagocytosis. The strict specificity of these antibodies partly explains the failure to produce a successful protective or curative serum for pneumonia. We do not yet know enough about variations and differences of the pneumococci, nor of the chemical and biological changes which they induce within the host. It is to be hoped that as our knowledge increases along these lines, we may be able to deal more effectively with the problem of the prevention and cure of pneumonia.

THE SYMPTOMOLOGY AND DIAGNOSIS OF PNEUMONIA.*

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Nothing much has been added to our knowledge of the symptoms of pneumonia since Auenbrugger and Laennec first described the physical signs about the year 1819. It is not my disposition to bore you with a discussion of the familiar symptomology of typical cases of pneumonia. Generally speaking, the clinical picture in any case is exactly similar to that in many other cases of the same condition, the sudden onset with chill, pain in the side, headache, high temperature, cough, rusty sputum, dyspnoea, herpes and leucocytosis. These symptoms, occurring in connection with dulness on percussion, increased fremitus, tubular breath-

5. Hastings, T. W. and Boehm, Emil: Journ. Exp. Med., 1913, XVII, 239.

6. Peabody, F. W.: *Ibid.*, XVIII, 1, 7.

7. Bernard et Mantoux Ed. Abstr., Jour. A.M.A., 1913, LX, 1794.

8. Clough, P. W.: Johns Hopkins Hosp. Bull., 1913, XXIV, 295.

9. Rachford, B. K.: Dis. of Children, 1912.

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ing and crepitant rales, are sufficient and familiar to you all. There are, however, pneumococcic infections of the lung which occasionally confront us with difficulties of solution, therefore it may be well to consider a few of these conditions. I think you will all agree with me when I say that the pneumonias occurring in children and the aged are often atypical, giving rise to symptoms which are frequently misleading. There are many explanations offered for the peculiar diversity of symptoms in infectious diseases attacking children. It is common knowledge that the nervous system of a child is more susceptible to toxemia than that of the adult; also children are difficult to examine and often refer their pain to parts unaffected. For this reason the child has been operated for appendicitis when pneumonia was the sole explanation for the abdominal symptoms. I have recently seen a child suffering from otitis who referred his pain to a tooth in the lower jaw.

Not rarely one sees pneumonia in children simulating symptoms of meningitis; this not infrequently occurs in the adult. It is claimed that this form of pneumonia, associated with delirium and convulsions, is due to the apical form of the disease, seen more often in children than the adult, and frequently very confusing. Again in children there is usually practically no sputum, very little cough and seldom rigor.

In reviewing the literature I have observed that the mistakes made in the majority of the cases of atypical pneumonia, reported in children, incorrectly diagnosed or mistaken for other diseases, have been due to neglect of an examination of the chest. The same thing may be said of senile pneumonia and of secondary pneumonias, occurring in chronic diseases. The physician has not had pneumonia in mind or has excluded it on account of an atypical history. One has but to bear in mind that sixty per cent. of all cases of pneumonia occur in children; the symptoms are not infrequently misleading. The chest should be examined in every case with a temperature. This precaution will often save embarrassment.

There are cases of pneumonia, for instance, abortive pneumonia, and the rare cases of fulminating pneumonia, which are almost impossible of diagnosis.

Speaking of fulminating pneumonias recalls some cases reported by McGowan and McNeill¹ collected from an industrial school near Edinburgh. There were twenty cases of the fulminating type, epidemic in character, showing a rapidly fatal issue. One of two boys went to bed well, and was found dead the next morning. The common clinical manifestations were a very sudden onset of high fever, headache, vomiting, herpes and some cough with loose blood stained sputum. The cases autopsied showed either acute general congestion or irregular

areas for consolidation. When sought for pneumococci were found in abundance in the lungs, but only in one case in the blood. Charles Macalister² describes four cases of death occurring in two hours in boys from an industrial school, which he attributed to pneumonia and recently Ernest Glynn³ reports two small epidemics of pneumococcic infection of the lung in a public institution. There were fifteen cases with four deaths. Two terminated fatally within seven hours after the onset of the first symptoms. The ordinary postmortem signs of pneumonia were completely absent. In two others, one showed definite pneumonic consolidation and in the other pneumonic consolidation had begun. In all the infection was primarily respiratory. Septicaemia could not be demonstrated but profound degeneration of the kidneys with thrombosis and hemolysis in the vessels of the lung and kidney were found. Clinically all the cases were atypical on account of the prominence of gastrointestinal and cerebral symptoms. The question arose, in the above cases where the pneumonia was fulminating, as to whether there was a factor other than the lung infection causing death. In one of Glynn's cases the thymus was hypertrophied and weighed over two ounces. McHowan and McNeil claim that their case of fulminating pneumonia had status lymphaticus. It is well known that patients with status lymphaticus die from very trivial causes, and it may not be too presumptuous to suppose that the pneumococcus infections may produce sudden death in this disease before physical evidence of pneumonia is present.

In the aged the same difficulties arise but more often due to lack of symptoms, the disease often begins insidiously without complaint on the part of the patient. In these patients there is usually some cough but little temperature. The cases may be afebrile. I recall a case in the City Hospital in New York, of a patient in the genitourinary clinic, who dropped dead in the ward. At autopsy one lung was found completely consolidated and in the other consolidation had begun. This patient had made no complaints and the chart revealed a temperature not over 99.2° at any time during his stay in the Hospital. However these symptomless form of pneumonia invariably show signs in the lungs on examination. In the asthenic where the patients are suffering from fatal chronic disease, repeated examinations of the lungs will prevent the chagrin not infrequently encountered at autopsy.

In cases of ambulatory pneumonia where the patient complains of very little besides slight cough, malaise and anorexia, one may neglect to examine the lungs, and of course the diagnosis is missed. These patients usually have a very slight temperature or none at all. On ex-

amination, the lungs usually show a few rales with a small area of consolidation at one base. Recovery is usually complete in a week or ten days under treatment with simple cough remedies. These patients frequently go about without consulting a physician.

DIAGNOSIS.

The diagnosis of pneumonia is seldom difficult, but mistakes are common and not always due to carelessness, and in a small minority the diagnosis is attended with much uncertainty. Mistakes arise: (1) where the signs are absent, here a careful history is very important; (2) where the early symptoms are cerebral; (3) where the symptoms are abdominal; (4) because certain of the specific fevers have a pneumonic onset; (5) occasionally acute pneumonic tuberculosis simulates pneumonia; (7) sometimes pleurisy with effusion will show increased fremitus and tubular breathing together with chill and fever; (8) rarely a subphrenic abscess will simulate pneumonia. I know of a case of postoperative gastroenterostomy for duodenal ulcer, develop cough, dyspnoea, chill and high temperature, tubular breathing, dullness on percussion and increased fremitus. For ten days this patient was thought to have pneumonia, but a needle revealed pus below the diaphragm. Here one could well bear in mind the researches of C. F. Hoover⁴, who has shown experimentally that where the diaphragm is pushed upward from below the subcostal angle on the affected side, during normal inspiration shows a greater excursion than that of the unaffected side. This never occurs in pneumonia. In empyema the diaphragm is pushed downward, here the excursion of the subcostal angle on the affected side is inward instead of outward. The explanation of this phenomena is shown to be due to the antagonism offered by the diaphragm to the scapular and intercostal muscles.

It might be well to recall an observation made by Dr. Hughlings Jackson on the absence of knee-kick in pneumonia. This reflex disappears about the third or fourth day to reappear upon the ninth. I have had no experience with this sign, however. In the differential diagnosis, the examination of the urine may be of some importance, as Hutchinson has shown that there is a marked diminution of sodium chloride in the urine in pneumonia, which persists for a day or two after the crisis.

We may conclude that 90% of all pneumonias with atypical symptoms can be diagnosed by a careful systematic examination. A small minority of the cases show no signs in the lungs. Should these patients survive, signs sooner or later develop and a correct diagnosis may be made.

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4. Hoover, C. S., *Arch. Int. Med.*, Aug., 1913, p. 214.

THE ALBUMIN CONTENT OF SPUTUM AND ITS VALUE IN DIAGNOSIS AND PROGNOSIS OF TUBERCULOSIS.*

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When Koch, in 1882, demonstrated the tubercle bacilli, enthusiastic clinicians for a time believed that search for this bacillus in secretions from the site of a lesion would determine absolutely the presence or absence of tuberculosis. Early experience, however, soon indicated that most careful examination for tubercle bacilli in discharges, later proven to be tuberculous, frequently failed to give positive results. In dealing with this class of cases the idea was generally accepted that such discharges contained the bacilli of tuberculosis but the number was not sufficiently great to enable the bacteriologist to find them with the methods ordinarily employed. In support of such views several instances could be cited where animal inoculation had shown the presence of the bacilli when direct microscopic examinations had failed. In routine clinical work, however, animal inoculation is generally impractical except in selected cases. Mixed infection that may kill the test animals before tuberculous lesions have time to develop are often present and difficult to eliminate; the length of time required by test animals to develop lesions characteristic of tuberculosis is such that valuable time is lost; besides test animals are by no means always infected when injected with exudates that can be proven to be of tuberculous origin.

Various methods of concentrating discharges without destroying the tubercle bacilli have been proposed with more or less success. Among such the use of antiformin probably deserves first place. We have used antiformin on several hundred negative sputa with the conclusion that aside from selected cases the method has very little practical value, because if the time required to treat sputum as required in the antiformin method be applied in judicious study of a well prepared slide, the results will be as reliable as when antiformin is used.

*From the Laboratory of Michigan State Board of Health.

Physicians formerly believed tuberculosis to be transmitted chiefly by inhalation. Their theoretical reasons for this opinion were various and need not be considered here. Accepting the theory that tubercle bacilli are generally inhaled directly into the lungs, entering the tissues from the lumen of the bronchi or alveoli, one might reasonably expect the specific germ to be found in the sputum from the very beginning of the disease, if sufficient concentration were obtained or the search were sufficiently prolonged.

Modern investigations indicate that pulmonary tuberculosis is not generally the result of tubercle bacilli having reached the lung through the lumen of the bronchi but that the infection appears first in the deeper structures and that tuberculous lesions are primarily closed lesions that become open only as the disease progresses.

Tubercle bacilli are discharged from open lesions but not from closed lesions. Within the lung a tuberculous lesion may be productive of considerable exudate, but so long as it remains closed the tubercle bacilli appear to be held back by the filter-like action of the surrounding tissue.

The facts are that after all known methods of isolating and identifying tubercle bacilli have been exhausted there still remains a number of cases of active tuberculosis from which tubercle bacilli cannot be demonstrated in the secretions by any method presently known.

THE ALBUMIN REACTION.

The albumin reaction in sputum has received considerable attention among the French workers during the past three years. The determinations have been mostly qualitative and the technic has been that originally employed by Roger and Levy-Valensi,¹ or some modification thereof. The sputum is collected in a dry recipient as free from saliva as possible. Sputum containing blood should never be used as the albumin contained in the blood serum always gives the reaction. The sample is mixed with an equal volume of water and acidified with a few drops of acetic acid to coagulate the mucin. The mixture is filtered through an ordinary filter paper and the filtrate is tested for albumin by boiling with either a little salt or nitric acid. In 1911, Roger² compiled from the literature and his own experience 1638 cases in which the sputum had been tested for albumin including 800 cases of tuberculosis in the second or third stage with negative albumin in only one case and certain features of the bacteriological findings in that case suggested the possibility of pseudo-tuberculosis. In 280 tuberculous patients in the first stage there were only two

giving a negative reaction among those properly tested and the diagnosis was made with some reserve in these. In 284 patients with non-tuberculous pulmonary or bronchial lesions a positive reaction was obtained in 144. He concluded that an absence of the albumin reaction excludes tuberculosis with practical certainty, that the reaction is an important accompaniment of tuberculosis but its presence is not pathognomonic of that infection.

Lesieur and Prirez³ investigated the sputum voided in various conditions for albumin content. They used five cubic centimeters of sputum diluted to twenty-five cubic centimeters with normal salt solution, added five or six drops of acetic acid, filtered and tested in the usual way. They found that of cases without physical signs which subsequently proved to be tuberculous 75 per cent. gave a positive reaction, that all cases with tubercle bacilli in the sputum were positive, that in miliary tuberculosis and pleurisy the result was not constant, the cases of acute lobar pneumonia reacted and that when the reaction persisted into convalescence a new focus or a complication was indicated. Acute broncho-pneumonia and acute pulmonary edema were also positive. On the other hand, in acute bronchitis it was usually negative; in chronic bronchitis and in emphysema always so. In cardio-renal cases a positive reaction was often seen.

Fishberg and Felberbaum⁴ found that the albumin reaction was not positive in every case of pulmonary tuberculosis. They concluded that the activity of the process has considerable influence on the intensity of the reaction. In active progressive cases the amount of albumin was greater than in quiescent or healing cases. In fibroid cases the amount was often infinitesimal or entirely absent.

Numerous other workers have studied the albumin reaction in sputum and agree that the presence of albumin indicates that it is not a superficial secretion but comes from some deep-seated inflammatory process. The reaction is independent of the presence or absence of tubercle bacilli and its intensity bears a distinct relation to the activity of the inflammation. The reaction is constantly present in pneumonia and pulmonary edema and generally absent in bronchitis and other superficial inflammations.

Gelderblom⁵ believes the presence of albumin in sputum to be coincident with a fresh process in the lung. He considers the rise and fall of the albumin content as an index to the course of the process and thus of value in prognosis. He found a rising albumin content to fall sharply following pulmonary hemorrhage and believes that the presence of albumin in the sputum

1. *Presse Medicale* April 20, 1910.

2. *Jour. A.M.A. ab. Vol. LVI, p. 1619.*

3. *Paris Medical*, 1911, Vol. IV, p. 29.

4. *Medical Record*, Oct. 21, 1911.

5. *Deutsche Med. Woch.* Oct. 9, 1913.

early in pulmonary tuberculosis indicates the blood-borne origin of such lesions.

Fullerton⁶ reported the examination of 100 cases and noted wide variation in the amount of albumin. He used the terms "abundant," "moderate," "slight," "trace," and "nil." He concluded that in a majority of cases of pulmonary tuberculosis the sputum contained albumin in considerable amount, but in a small proportion of cases little or no albumin was found; that a positive reaction occurred in various diseases of the respiratory tract; that the albumin reaction was not entirely reliable in diseases of respiratory tract and only of limited value in pulmonary tuberculosis.

Scott⁷ examined 85 cases with tubercle bacilli in the sputum and found albumin negative in 9.4% and doubtful in 27%. This would give positive albumin in only a little over 60% of tuberculous cases and unfavorable conclusions naturally follow.

In reviewing the literature on this reaction we have been impressed with the frequent references to "the intensity of the reaction" and the lack of agreement as to whether certain diseases give positive or negative results. With a test of this kind the personal equation is very great and what would be regarded as a negative reaction by one observer might easily be positive to another. The advisability of putting the reaction on a quantitative basis seems imperative to uniform results.

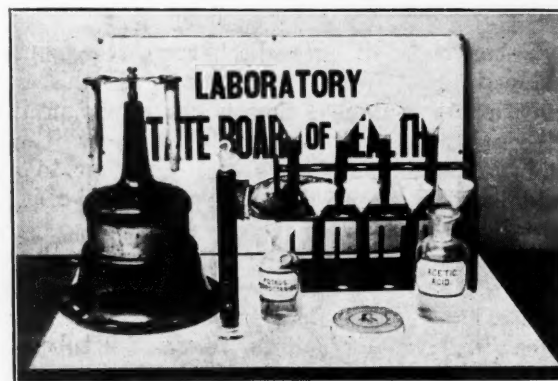
In 1912, Works⁸ published the result of quantitative examination of albumin in the sputa of 168 patients. He mixed with the sputum a three per cent. acetic acid solution, adding slowly and agitating until the mucin was coagulated, then added enough distilled water to make a 33 $\frac{1}{3}$ % dilution of the sputum. This mixture was thoroughly agitated, strained through gauze after which a few drops more of acetic acid was added to insure complete precipitation of mucin and the mixture filtered. Quantitative tests for albumin were made with Esbach's albuminometer as in urinalysis and the result multiplied by three to correct for dilution. He concludes that most active cases whether incipient, moderately advanced or far advanced show 0.2% or more albumin. Improved (slightly active) cases usually have less than 0.2% albumin.

The method employed by Works is undoubtedly an improvement over the qualitative methods previously proposed but possesses certain objectionable features. In the opinion of the writer the quantity of acetic acid should be specifically stated, as an insufficient quantity gives incomplete separation of mucous and excessive quantity disintegrates the leucocytes and prevents proper separation of pus proteins. We

also regard Esbach's solution as an improper reagent for albumin in a mixture so complex as is the average sputum. In many instances a precipitate may be produced with this reagent when true albumen can be shown to be absent. Picric acid, the active ingredient of Esbach's solution, is a general alkaloid reagent. It precipitates with peptones, urates, creatinin and other bodies that should not be measured as albumin. Works found that his method gave albumin reaction with normal saliva, a serious objection that we repeatedly have been able to confirm.

AUTHOR'S METHOD.

In January 1914, Holm and Himmelberger⁹ described a method for the quantitative determination of albumin that appears to give satisfactory results. A quantity of sputum, not



Physicians' Outfit for Albumin Determinations in Sputum.

less than ten cubic centimeters, is collected in a dry receptacle in the usual way. (Samples containing blood should be rejected, as blood invariably contains albumin.) After smears for microscopic examination have been made, a quantity of sputum not exceeding ten cubic centimeters is poured into a fifty cubic centimeter graduated glass-stoppered cylinder. To this is added three times its volume of water containing one per cent. acetic acid, diluting the sputum to twenty-five per cent. After vigorous shaking with the stopper in place, the mixture is filtered through filter paper directly into a graduated centrifuge tube and ten cubic centimeters collected. To this is added five cubic centimeters of five per cent. solution of potassium ferrocyanide in water and the tube whirled in a centrifuge for five minutes at average speed. The amount of albumin is most conveniently recorded in volume per cent., each one-tenth cubic centimeter on the tube being four per cent. by volume after correcting for the original dilution. Absolute accuracy is impractical in this work, so approximate results only need be recorded. If desired, the volume per cent. may be calculated to weight per cent. according to the method of Purdy for urinalysis.

6. Glasgow Med. Jour. July, 1912.

7. Jour. A.M.A., Feb. 8, 1913.

8. Jour. A.M.A., Oct. 26, 1912.

9. Jour. A.M.A., Vol. LXII, 20.

REPORT ON 1500 EXAMINATIONS.

Up to the present time we have employed the above method on something over 1500 sputa, including routine examinations and selected cases. The following table shows the findings

from 1,428 consecutive specimens taken since July, 1913. These samples represent cases suspected of being tuberculous as submitted by various practitioners in different parts of the state.

SPUTUM EXAMINATIONS.					
Albumin Reaction		Tubercle Bacilli			
		Present		Absent	
Absent		123	1— %	54+	590(1) ² (4) ³ (1) ⁷ (2) ⁹
Below 2% by volume	¹¹ (1) ¹³ 18		5+ %	10+	111(3) ¹ (2) ² (1) ³
Between 2% and 5% by volume	23		6+ %	6+	67(4) ¹
Between 5% and 10% by volume	¹ (1) 34		10— %	6+	69(5) ¹ (1) ² (1) ³
Between 10% and 25% by volume	¹⁰ (1) ¹ (2)109		31+ %	13—	138(10) ¹ (2) ² (2) ⁴ (4) ⁶ (2) ⁸
Between 25% and 50% by volume	¹ (1)113		33— %	8+	87(3) ¹ (3) ² (1) ³ (5) ⁴ (5) ⁶ (3) ⁸ (1) ⁹
Above 50% by volume	¹ (4) 46		13+ %	2—	20(4) ¹ (2) ⁵ (2) ⁸
Totals	346	100	%	100	1082

*1. Contained blood.

*2. Later examination showed tubercle bacilli present.

*3. Had previously shown tubercle bacilli in sputum.

*4. Abscess.

*5. Pulmonary edema.

*6. Pneumonia.

*7. Acid-fast bacilli, not tubercle bacilli, present.

*8. Pleuritic effusion.

*9. Stomach contents.

*10. Urine from tuberculous kidney.

*11. Feces from tuberculous intestine.

*12. Two of these were advanced cases of pulmonary tuberculosis. The first patient died before a second sample could be obtained. The second patient died eleven days after the sample with negative albumin was examined, but two subsequent examinations were made before the death of the patient, giving albumin 16% and 24% respectively, with tubercle bacilli very numerous. The third case gave albumin 1% and 1½% on subsequent examinations and appears to be at least temporarily an inactive infection. All three of the specimens giving negative albumin in the presence of tubercle bacilli have been small and rather unsatisfactory samples. The find-

ing of negative albumin where tubercle bacilli were present has not been duplicated in any case in our series.

*13. In every instance where albumin was found below 2% in the presence of tubercle bacilli, duplicate samples have been asked for. Second samples have generally shown albumin in larger quantities. One case gave as high as 70% within a week following a sample below 2%. It has been quite evident that most of our cases with such low albumin have been admixtures of saliva or other secretions not derived from the tuberculous lesion. Four cases have given below 2% albumin with tubercle bacilli present on two successive examinations. One of these has been previously referred to under *12. Another gave 6% albumin on a subsequent examination and was no longer followed. The third was from a case of tuberculosis of five years duration in a man of 44 years, showing very slight symptoms. This case recently came to our notice and only two examinations have been made at the time of this writing. The fourth case is somewhat interesting because of having changed from tubercle bacilli present to tubercle bacilli absent on microscopical examination while we were following the case. The findings have been as follows:

Patient C. D., South Haven. Physician, Dr. N. L. Goodrich.

Date	10-25	11-12	11-20	12-4	12-10	12-19	12-27	1-7	1-16	1-24	2-5	2-17	2-28
Tb. Bacilli	+	+	—	+	—	—	—	—	—	—	—	—	—
Albumin ..	1%	½%	Trace	24%	10%	—	16%	28%	—	—	8%	18%	—

The patient is past 40 years and gives a history of having been treated and cured of tuberculosis at the age of 18 and again at 25 years. The present attack was of about 8 months duration at the time of our first examination. Dr. Goodrich has informed us that the rise and fall in albumin corresponds closely to her symptoms.

One other patient that has changed from an open to a closed case occurred in the practice of Dr. C. E. Skinner, of Howell. In this case the following results have been obtained:

Date	1-10	2-5	2-10	2-18	3-2
Tb. Bacilli ..	+	—	—	—	+
Albumin	32%	4%	8%	12%	36%

The finding of tubercle bacilli occurred apparently toward the termination of a pneumonia and the concurrent pneumonia may be responsible for part of the first high albumin. However the case is not doing well and the prognosis should be guarded at this time.

It appears that before reliable conclusions may be drawn from low or absent albumin findings,

assurance must be had that the sample examined comes from the area in question. We have been able to show from cases of open pulmonary tuberculosis that the bacilli may be found in saliva, in water used for gargling the throat and even water used for rinsing the mouth. Such material would obviously be relatively free from albumin. Further, tuberculosis in a certain portion of a lung does not exclude other pathological conditions in different portions of the respiratory passages. One patient actually furnished in the same day a sputum free from tubercle bacilli and albumin and another containing a fairly large number of tubercle bacilli and 8% albumin. Such conditions are probably rare but we believe the possibilities they present offer satisfactory explanation for the low or absent albumin findings in exception to the general rule.

In studying a large number of sputa in connection with the albumin determination one is impressed with the high percentage of negative albumins in the most probable non-tuberculous cases, while in cases with clear physical signs the albumin is present quantitatively as in the open cases. Albumin appears to be entirely independent of the presence or absence of tubercle bacilli or of their relative number. There appears to be no constant relation between pus and albumin in sputum. We have found many samples highly purulent to be free from albumin while others comparatively free from pus have been very high in albumin. As a rule a sputum with markedly disintegrated pus cells is associated with considerable albumin but even here we find many exceptions.

Up to the present time no satisfactory physiological explanation for the presence or absence of albumin in sputum under various conditions has been offered and in the absence of such the diagnostic and prognostic value of the determination must remain largely speculative.

The albumin in tuberculous secretions is undoubtedly of the nature of an inflammatory exudate and the quantity is a measure of the inflammatory reaction. The reliability of quantitative determinations, however, must be judged with due considerations for other substances such as saliva, nasopharyngeal discharges, bronchial secretions, vomitus and other materials that may enter into the composition of sputum, diluting or otherwise modifying the quantitative results.

Scott called attention to a comparatively low albumin finding in a case that terminated fatally within a short time after examination. We have encountered two similar cases and consider such findings in accord with our theory. A tuberculous lesion may give low albumin either because it is inactive or because the tissues are too weak to respond with proportionate inflammatory reaction. High albumin means a vigor-

ous reaction and such results generally though not necessarily follow extensive injury.

CONCLUSIONS.

Our findings indicate that albumin is present in the sputum of practically all cases of unquestionable pulmonary tuberculosis and that in over 80% of these the amount is above 10% by volume. Albumin is also present in all cases of pulmonary abscess, broncho and lobar pneumonia and pulmonary edema. In chronic rhinitis, pharyngitis, laryngitis, bronchitis and asthma albumin is generally absent or present only in traces. In acute conditions the findings are less constant. While an absence of albumin is the rule in all superficial inflammations of mucous membranes, abrasions or lacerations of the surface epithelium are occasional accompaniments to such cases and give rise to serous or bloody exudates that contain albumin in abundance. An absence of albumin we believe excludes active tuberculosis as the source of that particular sputum. This statement may seem radical in view of the fact that over 50% of the sputa suspected of being tuberculous, with tubercle bacilli absent show negative albumin. However, the opinion appears justifiable with the strict understanding that it does not apply to the patient as a whole but is limited to the source of the sample examined.

REPORT OF EXPERIMENTS TO TEST THE TOXICITY OF MOTHER'S MILK AFTER ADMINISTRATION OF ACETANILIDE.

BEATRICE A. STEVENSON, M.D.,
DETROIT, MICH.

(From the Grace Whitney Hoff Laboratory, Women's Hospital, Detroit.)

Mrs. D., for the relief of a sick headache, took a wafer containing 4 grains of acetanilide and 1 grain of caffeine. This was at nine o'clock in the evening. At two o'clock the next morning, five hours later, she nursed her four months old baby. At 7:45, the same, morning, the child died.

The physician who was called makes the following statement: "The baby was alive and apparently in perfect condition when the mother got up in the early morning, but when the mother went back to see that the child was covered she found it dead. The baby was well and happy the day before and had never been sick. The only cause of death that I could discover was the headache wafer taken by the mother the night before."

It is well known that milk acquires a foreign taste from changes in the food of the animal producing it. The peculiar taste of milk from cows fed on garlic is an example. This is proof

that foreign bodies may pass into the milk, although Holt believes that few of the drugs supposed to affect the child through the milk really do so. If the milk is poor in quality elimination of drugs is more likely to take place. The most important drugs known to be so eliminated are belladonna, opium and morphine, alcohol, the iodides and bromides, mercury only after prolonged use and then irregularly, most of the saline catharics, arsenic and the salicylates occasionally. Bismuth, antimony, zinc, lead and iron have also been found in the milk.

So far as could be discovered, the fate of acetanilide in the system is as follows: As soon as introduced it is rapidly absorbed and as rapidly excreted by the kidneys, disappearing within 24 to 36 hours after its administration. Acetanilide itself does not appear in the urine except after very large doses. It is represented by its derivatives, paramido-phenol and acetyl-paramido-phenol.

To ascertain whether acetanilide did appear in the milk of a nursing mother and if so, whether in sufficient quantity to cause the death of an infant, the following tests were made in the Grace Whitney Hoff Laboratory connected with the Woman's Hospital. The babies were put on artificial food and the drugs were administered to the mothers and specimens obtained as follows:

CASE 1, SALLIE.

Age of baby	Time of admin.	Dose
3 months	10:30 p. m., Jan. 25	Acetanilid gr. IV Caffeine gr. I
Specimen	Time taken	Result
Milk	9 p. m., Jan. 25	Control
Milk	2 a. m., Jan. 26	Negative
Milk	6 a. m., Jan. 26	Faint trace
Milk	9 a. m., Jan. 26	Faint trace
Milk	12 noon, Jan. 26	Negative
Urine	6 a. m., Jan. 26	Trace
Urine	12 noon, Jan. 26	Negative

CASE 2, SYLVIA.

Age of baby	Time of admin.	Dose
2 months	10:30 p. m., Jan. 25	Acetanilid gr. IV
Specimen	Time taken	Result
Milk	9 p. m., Jan. 25	Control
Milk	2 a. m., Jan. 26	Negative
Milk	6 a. m., Jan. 26	Faint reaction
Milk	9 a. m., Jan. 26	Negative
Milk	12 noon, Jan. 26	Negative
Urine	6 a. m., Jan. 26	Negative
Urine	12 noon, Jan. 26	Negative

Since it seemed possible that the decided color changes in Case 1 might be due partly to the combination with caffeine it was decided to give that patient acetanilide alone, to give Case 2 acetanilide and caffeine and to put a third patient on caffeine alone.

This third patient showed considerable variation in color of specimens on the addition of the reagents but no red tinge.

In Cases 1 and 2 the results in the second test were the reverse of those in the first, as follows:

CASE 1, SALLIE.

Age of baby	Time of admin.	Dose
3 months	9:45 p. m., Jan. 26	Acetanilid gr. IV
Specimen	Time taken	Result
Milk	9 p. m., Jan. 26	Control
Milk	2 a. m., Jan. 27	Negative
Milk	6 a. m., Jan. 27	Faint reaction
Milk	9 a. m., Jan. 27	Negative
Urine	2 a. m., Jan. 27	Negative
Urine	6 a. m., Jan. 27	Negative

CASE 2, SYLVIA.

Age of baby	Time of admin.	Dose
2 months	9:45 p. m., Jan. 26	Acetanilid gr. IV Caffeine gr. I
Specimen	Time taken	Result
Milk	9 p. m., Jan. 26	For control-trace
Milk	2 a. m., Jan. 27	Fainter trace
Milk	6 a. m., Jan. 27	Trace
Milk	9 a. m., Jan. 27	Trace
Urine	2 a. m., Jan. 27	Very faint trace
Urine	6 a. m., Jan. 27	Very faint trace

In this test, Case 2 shows a trace in every specimen, even in the control, and as the case reacted very slightly in the first test it was decided to give each of the two cases a dose of acetanilide alone for two nights in succession in order to determine whether or not the late positive reaction in Case 2 was due to accumulation. The results were as follows:

CASE 2, SYLVIA.

Age of baby	Time of admin.	Dose
2 months	9 p. m., Jan. 31	Acetanilid gr. IV
Specimen	Time taken	Result
Milk	9 p. m., Jan. 31	Negative-control
Milk	2 a. m., Feb. 1	Negative
Milk	6 a. m., Feb. 1	Negative
Milk	9 a. m., Feb. 1	Faint reaction
Milk	12 noon, Feb. 1	Negative
Milk	3 p. m., Feb. 1	Negative
Milk	6 p. m., Feb. 1	Negative
Urine	2 a. m., Feb. 1	Negative
Urine	9:15 a. m., Feb. 1	Negative
Urine	12 noon, Feb. 1	Negative

SAME CASE, SYLVIA.

Age of baby	Time of admin.	Dose
2 months	9 p. m., Feb. 1	Acetanilid gr. IV
Specimen	Time taken	Result
Milk	9 p. m., Feb. 1	Negative
Milk	2 a. m., Feb. 2	Negative
Milk	6 a. m., Feb. 2	Negative
Milk	9 a. m., Feb. 2	Negative
Milk	12 noon, Feb. 2	Negative
Urine	9 p. m., Feb. 1	Negative
Urine	6 a. m., Feb. 2	Negative
Urine	9 a. m., Feb. 2	Negative

It is very evident that there is no accumulation in this case. In the other case the test was of no value as the patient left the hospital after

the first administration, so the first case of all, Sallie, was given another dose to test for accumulation. This case was not entirely satisfactory as there had been an interval of four days between doses.

CASE 1, SALLIE.

Age of baby	Time of admin.	Dose
3 months	9 p. m., Feb. 1	Acetanilid gr. IV
Specimen	Time taken	Result
Milk	9 p. m., Feb. 1	Negative
Milk	2 a. m., Feb. 2	Negative
Milk	6 a. m., Feb. 2	Negative
Milk	9 a. m., Feb. 2	Negative
Milk	12 noon, Feb. 2	Negative
Urine	9 p. m., Feb. 1	Negative
Urine	6 a. m., Feb. 2	Negative
Urine	9 a. m., Feb. 2	Negative
Urine	12 noon, Feb. 2	Negative

There is no accumulation.

In all the foregoing experiments the reaction of the *urines* to the reagents was in each case definitely positive or negative, but the reaction of the milk specimens was not so satisfactory. The specimens from one patient were not uniform in color when first taken and there was considerable confusion after the addition of the reagents owing to the many shades and tints that were exhibited. It was decided that this might be due to the presence of the casein, so in the next and final set of experiments hydrochloric acid was added to each specimen and it was then boiled and filtered. With the comparatively clear filtrate thus obtained it was possible to be very positive about the reaction. The results in the final tests were as follows:

CASE 3, LILLIE.

Age of baby	Time of admin.	Dose
4 weeks	9 p. m., Feb. 6	Acetanilid gr. IV
Specimen	Time taken	Result
Milk	9 p. m., Feb. 6	Negative-control
Milk	2 a. m., Feb. 7	Negative
Milk	6 a. m., Feb. 7	Negative
Milk	9 a. m., Feb. 7	Negative
Milk	12 noon, Feb. 7	Negative
Milk	3 p. m., Feb. 7	Negative
Milk	6 p. m., Feb. 7	Negative
Urine	9 p. m., Feb. 6	Negative
Urine	6 a. m., Feb. 7	Negative
Urine	9 a. m., Feb. 7	Negative
Urine	12 noon	Negative
Urine	3 p. m., Feb. 7	Negative
Urine	6 p. m., Feb. 7	Negative

SAME CASE.

Age of baby	Time of admin.	Dose
4 weeks	9 p. m., Feb. 7	Acetanilid gr. IV
Specimen	Time taken	Result
Milk	9 p. m., Feb. 7	Negative
Milk	2 a. m., Feb. 8	Negative
Milk	6 a. m., Feb. 8	Negative
Milk	9 a. m., Feb. 8	Negative
Milk	12 noon, Feb. 8	Very faint reaction
Urine	9 p. m., Feb. 7	Negative
Urine	6 a. m., Feb. 8	Negative
Urine	9 a. m., Feb. 8	Negative
Urine	12 noon, Feb. 8	Very faint reaction

CASE 4, MOLLIE.

Age of baby	Time of admin.	Dose
5 weeks	9 p. m., Feb. 6	Acetanilid gr. IV Caffeine gr. I
Specimen	Time taken	Result
Milk	9 p. m., Feb. 6	Negative-control
Milk	2 a. m., Feb. 7	Negative
Milk	6 a. m., Feb. 7	Negative
Milk	9 a. m., Feb. 7	Negative
Milk	12 noon, Feb. 7	Negative
Milk	3 p. m., Feb. 7	Negative
Milk	6 p. m., Feb. 7	Negative
Urine	9 p. m., Feb. 6	Negative
Urine	6 a. m., Feb. 7	Negative
Urine	9 a. m., Feb. 7	Negative
Urine	12 noon	Negative
Urine	3 p. m., Feb. 7	Negative
Urine	6 p. m., Feb. 7	Negative

SAME CASE, MOLLIE.

Age of baby	Time of admin.	Dose
5 weeks	9 p. m., Feb. 7	Acetanilid, gr. IV Caffeine gr. I
Specimen	Time taken	Result
Milk	9 p. m., Feb. 7	Negative
Milk	2 a. m., Feb. 8	Negative
Milk	6 a. m., Feb. 8	Negative
Milk	9 a. m., Feb. 8	Negative
Milk	12 noon, Feb. 8	Very faint reaction
Urine	9 p. m., Feb. 7	Negative
Urine	6 a. m., Feb. 8	Negative
Urine	9 a. m., Feb. 8	Negative
Urine	12 noon, Feb. 8	Negative

END RESULTS.

In this last set of experiments the milk and all the urine secreted for thirty consecutive hours was obtained for the tests. The precipitation of the casein obviated the confusion in the color reactions.

In the 24 specimens of milk and 20 specimens of urine examined there was a very faint reaction in but three specimens, these reactions occurring in thirty hours after the first and fifteen hours after the second dose.

The babies began nursing as soon as the experiments were concluded and none of them showed any ill effects.

CONCLUSIONS.

Up to this time there is apparently no record of the finding of acetanilide derivatives in mother's milk. From this set of experiments it would seem that acetanilide derivatives are at times eliminated but that more frequently there is no trace of them. The quantity found in each case was so minute that it could only be detected by holding the specimen against a white background. The time of the first appearance of the reaction after the administration of a dose of 4 grains varied from seven to fifteen hours. The baby of Mrs. S. nursed five hours after the mother took the same dose and not again before its death. Was this mother's milk so poor in quality that it was more like an ex-

cretion, so that the drug was eliminated in greater quantity and more rapidly? This seems hardly reasonable since it is stated that the baby was well nourished and had never been sick.

The symptoms mentioned in the recorded cases of acetanilide poisoning are cyanosis, prostration, dyspnoea, excessive restlessness, increased perspiration and coldness of the extremities. Surely a mother would have noticed these marked symptoms if they had been present when she examined her baby 15 minutes before its death. There is not a recorded case of death from acetanilide poisoning without symptoms.

PELVIC INFECTIONS.*

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The frequency of pelvic infections, with their high mortality, makes this subject of sufficient interest to bring it up for discussion before our society.

We have primarily two classifications, viz: those occurring with parturition and those independently of it. It is probable that puerperal infection has occurred as long as children have been born. Many evidences are to be found showing that it existed, and that means of preventing it were adopted, among the primitive savages. Four hundred years before Christ, Hippocrates described cases of it so accurately that the words could well be read in a modern classroom.

Not, however, until the second half of the seventeenth century were the first authentic reports of the epidemic disease given. In 1660, in Paris, at Hotel Dieu, two thirds of the women delivered died. And so this terrible disease raged, until as late as 1842. Vienna statistics show that the mortality of the women varied that year with the months, from eighteen to thirty-one per cent.

And now at a time when only the larger number of deaths was a positive fact and everything else in question, unexplained and doubtful, Semmelweis, a young assistant in the clinic at Vienna, as the result, not of accident, but of close observation, hard work and study, announced, in 1847, that puerperal fever is caused by the absorption into the blood, from the genitals, of *decomposed animal matter* from any source; that the hands, or any article brought into the genitals, may be the carriers of same. If, for the words *decomposed animal matter*, be substituted the word bacteria, the definition of puerperal sepsis is perfect as we understand it today.

With the cause he sought the remedy and instituted the washing of hands, cleansing of fin-

ger nails, plus the use of chlorine water or chloride of lime solution. The results were dazzling. The following year, 1848, the mortality dropped to 1.27%. To Semmelweis, then, an obstetrician, is due the credit of pointing the correct way to modern antisepsis and asepsis, years before the germ theory was born.

TYPES OF PELVIC INFECTIONS.

Since then we have come to recognize many types of pelvic infection, the great majority of which are covered by gonorrheal and puerperal infections. Others are the parasitic, external, cutaneous and glandular groups. In order that we may get a complete and clear conception of the way in which different forms of pelvic infections are developed and of their treatment, we will endeavor to study them, not according to the classification of that famous pair, pelvic peritonitis and cellulitis, by which the evolution and treatment were so long clouded, but according to our present knowledge of pathology, bacteriology, symptomatology and individual resistance.

I have here some charts prepared, showing fairly well the various types of pelvic infections, how they spread and how to differentiate them: viz.

MODES OF TRANSMISSION:

Exogenous.
Endogenous.

TYPES OF INFECTION—(Bacteria.)

Sterptococcic pyogenes.
Diplostreptococcus puerperalis.
Streptococcic pyogenes.
Diplococcus lanceolatus pneumoniae.
Staphylococcus aureus and albus.
Bacillus coli commune.
Gonococcus of Neisser.
Bacillus pneumoniae of Friedlander.
Bacillus pyocyaneus.
Bacillus proteus.
Bacillus aerogenes capsulatus.
Bacillus fusiformis and spirilla (hospital gangrene).
Bacillus typhosus.
Bacillus tetani.
Bacillus anthracis.
Bacillus diphtheriae.
Bacillus influenzae.
Chancroid Bacillus of Darcrey.
Tuberculosis.

ATRIA OF INVASION:

Vagina.
Cervix.
Uterine Surface.
Tubes.
Peritoneum.
Circulation.

ROUTES OF TRANSMISSION:

Lymph spaces.
Lymph vessels.
Blood vessels.
Continuity of tissues.

This paper will deal principally with infections, following parturition (abortions, miscarriages, curettements) and gonorrhea.

Puerperal infection is a surgical wound infec-

*Read before the Wayne County Medical Society, Surgical section, November 24th, 1913.

tion, the same germ attacking the structure and producing the pathology; many variations existing, however, depending upon the atrium and type of infection, demand special consideration.

The most common atrium of puerperal infection is through the vagina. The only wonder is that it does not occur oftener since these are lesions in a zone that is extremely hard to keep aseptic. The reason that infection does not occur oftener is that the field offers a high grade of resistance, which nature prepares by the coffee-damming, infiltration, edema, and swelling, which precedes parturition. Hence the rarity of infection of the cellular tissue of the perineum and vagina.

The next common field of infection in this region is through the lacerated cervix, a structure more highly supplied with lymphatics than any other part of the body. These lymphatics lead to the cellular tissue of the broad ligaments. Tissue richly supplied with lymphatics admits of frequent and rapid transmission of infective material.

Another field of infection, is the uterine cavity proper (at placental attachment, or following curettement). Here we have—what? An open wound, leading directly into the blood stream with an excellent opportunity for the development of a thrombophlebitis. An effort has been made to divide infections clinically into three classes:

Sapremia, meaning septic intoxication.

Septicemia, meaning absorption into the blood of living ferments (bacteria), bacteremia.

Pyemia, meaning pus in the blood, metastatic bacteremia.

This classification should not be made since these infections do not exist alone but are combined.

CONDUCT OF INFECTIONS.

Now as to the conduct of different infections. Among the infections that occur independently of parturition, mention is to be made of the colon bacillus vaginal infection, which is found in children, producing a discharge of pus, and lasting fifteen or twenty years. Pneumococcal infection, too, is common in the vagina of children; but the most important, on account of its frequency and severity, is gonorrhea.

The micro-organism of gonorrhea does not produce a cellulitis or a phlebitis. The Neisserian infection having once entered the tube, which it does only by continuity of tissue, following the mucous membrane from the vagina through the uterus to the tube, produces a pyosalpinx, destined always to be one. Both ends are sealed, the uterine end being closed by the peritubal inflammation and the distal end by agglutinations of the fimbriae.

In affections occurring with parturition we have, generally, either a staphylococcal, strep-

tococcal or colon bacillus infection. The latter, when present, usually is associated with the streptococcus or staphylococcus.

An infection of staphylococcal origin passes through the lymph spaces slowly, often arrested in loco, producing circumscribed abscesses in the uterine body, a favorite location being the cornu, or a circumscribed accumulation of pus in the broad ligaments, or the cellular tissue of the peritoneum. The condition is not unlike those infections so common on the body surface—boils, pustules, etc.

How different from the conduct of either the gonococcal or the staphylococcal infections is the one of streptococcal origin. These latter are extremely fatal, and seldom localize. They pass so rapidly through the blood stream that when injected into the uterus of an animal the organism has been demonstrated to be six minutes later in the liver.

CLINICAL FINDINGS.

With these truths in mind then, let us see what we find clinically. A woman is confined, or has an abortion, or a curettement. The next or the second day she has a chill with temperature 104 degrees or more, pelvic pain, as a rule, no vomiting. Within three or four days she dies, or the chills recur. They will continue for weeks and the pain increase in severity. Upon vaginal examination we find the uterus is fixed, and on one or both sides is a hard mass, fixed and immovable. The whole thing is as if set in masonry. What is the matter? An infection through the cervix extending into the cellular tissue and involving the broad ligaments. Aside from the general rules for treatment of all pelvic infections, which will be discussed later, what is to be the management of the case? With the formation of the fluctuating abscess, simply incise and drain. That is all; treat the same as an abscess of the breast or thigh.

Another clinical picture: Infection of the veins on the placental base—infection of the uterus. The day following delivery patient has a normal temperature, feels well until end of first week or as late as the second or beginning of the third, and one believes the patient has practically recovered, when there is a chill, a choking sensation, with interference in the breathing, and a sense of impending danger. The doctor is called and finds the temperature at 105 degrees, heart on a rampage, patient anxious and restless. A primary clot has been dislodged, and very soon the patient dies; or, following the chill there is a temperature ranging from subnormal to 105 degrees. The fever pursues an irregular course with marked remissions; pulse is rapid, 110 to 150. There is no evidence of metastasis; abdominal findings are negative, and in the pelvis there is no ten-

derness. The uterus is movable and there is possibly a slight indistinct thickening. In fact, though, all physical findings may be negative, and one may assume only from the clinical history that she has had a vein infected.

The surgical management has not as yet been settled. It is my opinion that the pelvis should be left severely alone, since in the rapidly advancing thrombosis we are powerless to stop the process, while in the localized types which are not actively virulent, the body resistance can be fairly well depended upon to master the situation. I would, however, recommend the use of autogenous vaccines, also as a preventive measure patients be allowed to move about in bed very early and very freely after delivery.

In another variety to be considered, following parturition or abortion, we have infection of the uterine cavity surface, passing on upward to the next surface by continuity, an infection of the mucosa of the tubes. When the infection has reached the tubes, usually the fimbriae becomes agglutinated, and through the lymphatics that lead back again into the broad ligament, the process terminates in the ligament. In some cases, however, the infective material passes along the surface of the fimbriated end of the tube into the pelvis, causing the only true type of pelvic peritonitis, except from a perforated uterus or a ruptured pus tube a like result will be obtained. This is a surface infection of the peritoneum and has not anything like the virulence, nor does it require the same treatment that the subperitoneal infections do.

In the subperitoneal infections it is useless to perform a laparotomy, because one cannot get into the subperitoneal cellular tissue where the pus is situated; while in the true pelvic peritonitis, all one needs to do is to provide drainage through a tube. This procedure is of much value and can best be accomplished by opening the Douglas pouch, and letting the fluid escape through the vagina. A sack of this kind cannot be enucleated as it is only pelvic peritoneum. Abscess in the cul-de-sac from any cause should be incised and drained.

In gonorrheal pus tube the only treatment of any use is extirpation. Drainage is useless, since the tube, having its diseased mucosa and both ends sealed, only refills, and unless they are removed, the patient, in spite of any conservative measures, goes through life a partial or complete invalid. I repeat, that without a mutilating operation complete recovery in these cases is about the rarest thing in surgery. The physical signs may be so slight that the patient is often regarded as a victim of neurosis, and it is only upon opening the abdomen that one finds justification for her complaints. In such cases operative measures are quite successful, and, freed from the chronic pains, the nervous system may return

to the normal condition. With hydrosalpinx (which never follows gonorrheal infection but is one of the end results of other infections, streptococic and staphylococic, which have undergone such changes as to become sterile) freeing the distal end of the tube and stitching the ends of the fimbriae so as to avert them produces an ectropion, whereby one preserves the possibility of pregnancy, since the relief of tension reduces the congestion, and the uterine end of the tube again becomes patent.

ABORTIONS.

In dealing with an abortion that came on without being induced, that is, without having any infective material carried into the uterus to induce it, treat it as an abdominal wound—keep the hands out, make no examination, never use a douche, protect the vulva with antiseptic dressings, and let the patient alone.

With induced abortion one has an entirely different thing. Here, as early as possible, dilate the cervix, and without laceration clean out the uterus of every portion or remnant, but never cross the threshold of the vagina until ready to go to the dome of the uterus.

TREATMENT.

Treatment of all pelvic infections is based upon general principles. Everything that will improve the woman's general health will help her throw off the disease, and the attendant should count no effort lost that will increase her resistive powers. Nourishing food is necessary; fresh air is important; sleep is a prime necessity; visitors are excluded; and in puerperal cases nursing of child stopped. An occasional laxative is ordered in prolonged cases. For the fever nothing need be done, excepting cold packs or ice bags; bathing is too fatiguing; medicines are very sparingly used, yet it is my desire to mention one old but very valuable drug, that is not used nearly as much as it should be. I speak of ergot. It has been my custom to use Ergotole, each minim of which represents $2\frac{1}{2}$ grains of select black Spanish ergot. This, given hypodermically every two hours, in doses varying from 15 to 45 minims, its effect is at the maximum in about 30 minutes and lasts one hour. It is particularly indicated in all the bacteraemias before pus formation, being a powerful stimulant to the vaso-motor centers, causing a tonic spasm to the muscular walls of the blood vessels accompanied by rise of arterial pressure and slowing of the heart beat. Of course, this, like other therapeutic agents, is only to be used in conjunction with proper surgical measures. In the acute stages vaccine treatment and should be instituted early. A bacteriologic diagnosis should be made. A blood culture with a two or four days incubation will usually make it possible, even when the culture

from the contents of the uterus is made. The latter procedure, however, should never be neglected. In cases in which the temperature does not fall but remains stationary after a fair trial of the vaccines, there is usually a walled off pocket of pus present, which if found and opened, will be followed by a positive phase and a prompt fall of temperature to normal.

Antistreptococcic serums have been found not to be as useful as was hoped for, but each dose of vaccine may be alternated with a dose of antistreptococcic serum. Large amounts of water introduced into the body are useful in supporting the embarrassed heart, diluting toxins, and promoting excretions.

Local treatment is absolutely contra-indicated in the acute stage. Internal examination is made very gently, except at the very outset, when portions of the retained secundines, or a blood clot, is present. They are to be removed preferably with the finger; also, a copious irrigation of the uterus with an iodine solution may be given. The cul-de-sac is never irrigated; pus tubes are enucleated not earlier than a year and, if of streptococcic origin, often several years must elapse before a perfectly safe operation can be done.

In meta-static bacteremia-(pyemia), collections of pus, whether in the pleura, joints, or peritoneal cavity, must be evacuated on ordinary surgical lines.

And finally, in the care of these cases, I would emphasize the importance of bearing in mind the intimate relation of the genital tract to the terminal reservoirs of the urinary and alimentary tracts, which permit of easy communication of disturbances and pathological conditions.

919-922 J. Henry Smith Bldg.

SYPHILIS OF THE NERVOUS SYSTEM.*

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Contrary to the general belief that syphilis of the nervous system was not recognized in the past centuries, except as it occurred in connection with syphilitic disease of the osseous tissue in close proximity with the cerebrospinal nervous system, we find in the oldest monographs on syphilis references to conditions which were undoubtedly known to be syphilitic disease in the central nervous system. Long before the greater epidemic of syphilis in Europe took place was paralysis of the extremities attributed to syphilis of the nervous system by a number of Mexican physicians. Paracelsus in his work 'Von der Franzoesischen Krank-

heit" in 1530 describes brain syphilis. In Morgan's dissertation in 1766 we find a description not only of syphilitic disease of the brain but also of gummatous leptomenigitis and syphilitic cerebral-endarteritis. About the same time Balloy describes hemifacial palsy due to syphilis and so there are many other references until finally in the nineteenth century Schützenberger, Griesinger, Westphal, Virchow, Heubner and Charcot paved the way to our knowledge of syphilitic disease of the nervous system of the present time. Of particular interest in this connection was the work of Virchow on syphilitic meningitis and gummata and that of Heubner on syphilitic disease of the vascular system of the brain.

It has long been recognized that syphilis is an infectious disease and numerous varieties of fungi and bacteria have been described by various investigators as the specific organism of the disease, but not until Schaudin found the *Spirochaeta pallida* was there much interest shown in these various claims. Schaudin's discovery was promptly confirmed by Eposchen, Busche, Fischer, Metschnikoff and Raux, who demonstrated the specific organism in the primary lesions and in the liver, spleen and the blood in acquired and congenital syphilis. Very soon was the organism demonstrated in the central nervous system and in the spinal fluid in acquired and congenital syphilis and at this time no one doubts that the *spirochaeta pallida* is the specific organism of syphilis wherever it may occur and in proof thereof is its constant existence in fresh syphilitic products and its absence in nonsyphilitic disease. Until quite recently pure cultures of the syphilitic organisms and the production of syphilis by these had not been successfully carried out, but Noguchi has accomplished this.

While it is somewhat difficult to judge accurately as to the frequency of syphilis of the nervous system, one working in the field of neurology and in a neurologic clinic, is impressed with the importance of the more recent laboratory tests for syphilis and the routine application of them in all cases irrespective of the symptom complex which they may present. There is probably no field in medicine wherein similar diseased pictures may arise from so many different causes as in the domain of the nervous system or where a single etiological factor may give rise to so many dissimilar pictures. It is only within comparatively recent times that apparently dissimilar diseases have been grouped under one etiological head. The dissimilarities in clinical expression within the nervous system have been so striking as to obscure the fundamental underlying causative factor. The dividing lines between the lesions of hereditary syphilis, acquired syphilis and so-called meta-syphilis are becoming slowly prominent and al-

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ready it seems strange that spinal and cerebral syphilis on the one hand, should ever have been considered different from tabes and general paresis on the other. Since we believe that tabes and general paresis not only rest upon a syphilitic basis but are due to the activity of the spirochaeta pallida, the variety of syphilitic disorders showing clear clinical entities has been enlarged both in the neurological and in the psychiatric clinic.

Acquired syphilis of the nervous system, early or late, makes up a large per cent. of the clinical material in a neurological practice. Erb gathered from 10,000 cases in his private practice in men over 25 years old exclusive of tabes 21.5 per cent. who had had a syphilitic infection. Statistics collected by the Prussian government in 1900 showed 11,000 cases of recent syphilitic infection in Prussia. Neisser's calculations showed that every fourth man who marries after the age of thirty has had a syphilitic infection.

The frequency of syphilis of the nervous system is shown by the statistics of Nonne. In five thousand five hundred patients treated in private practice for nervous disease, there were 85 cases of syphilis of the nervous system. Out of 72,180 admitted in the clinic for internal medicine there were 282 diagnosed as syphilis of the nervous system. In another medical clinic there were 104 in 9,936 patients diagnosed as syphilitic disease of the nervous system by the same authority. All of these either gave a history of a syphilitic infection or presented typical clinical pictures. The Wassermann test was at this time not used. From this, one may deduct that in a neurological practice 1.5 per cent. of the cases are syphilitic in origin, while in the general medical clinic 0.4 per cent. of the patients are suffering from syphilitic disease of the nervous system. In all of these figures tabes and general paralysis are excluded. These numbers would be much greater if the Wassermann test could have been applied. Fournier found in 1,085 cases of syphilitic disease of the nervous system 77 cases of spinal, and 406 cases of cerebrospinal syphilis, according to the general statistics cerebral syphilis is about eight times more frequent than spinal syphilis. Erb's experience is that tabes is ten times more frequent than any other syphilitic disease of the spinal cord. The statistics of some of the larger clinics of Europe show a marked increase in the occurrence of syphilis of the nervous system in the period between 1903 and 1907.

The view that syphilis attacks the nervous system largely in the tertiary period has long been abandoned. Nannyn showed that 40 per cent. (out of 335 cases) occurred in the first three years and that from this time on the number of cases diminished from year to year and after ten years it is exceptional when the

central nervous system becomes diseased. It is the experience of nearly all neurologists in this country and abroad that many cases occur between 11½ months to 11½ years after the infection. (Tabes and paresis being excluded).

Clinically and with reference to the pathological anatomy of syphilis of the nervous system we have formerly and do now recognize two distinct types: 1. The symptom complex due to pathological changes in the vascular system of the cerebrospinal nervous system and 2, that clinical picture due to the formation of gummata. The former may exist independently. In fact, only one or a few vessels in a single locality may be involved. It is doubtful that a gumma formation can take place without the involvement of the vascular system, it being primarily a periarthritis gummosa. The vascular form of cerebral syphilis presents clinically the symptom complex due to an arteritis (Endarteritis, periarthritis). This is separated into an inflammatory process such as we find in the larger vessels of the brain membrane and is characterized by a cellular exudate (periarthritis) and the noninflammatory form where the exudate is absent and there are no other anatomical changes save those in the vessel walls (Endarteritis). The latter presents in a general way quite a constant symptom complex, the former, on the contrary, great variations depending upon the extent and location of the pathological process. So in cerebral syphilis, whether it is a meningitis, a meningoencephalitis or a meningoencephalitis gummosa, or the process is a basilar meningitis with its characteristic cranial nerve palsies or a lesion of the meninges of vertex with epileptiform seizures there is only an anatomical difference and a difference in the extent of the lesion. The same holds good with the isolated gumma.

The present conception of spinal syphilis (meningomyelitis syphilitica) is based upon the same principle as brain syphilis. The clinical differentiation of the vascular or the meningomyelitic form is less apparent, while there are cases in which the vascular changes predominate; in others it is difficult clinically to separate this form from the more extensive degenerative process. The symptoms are of course dependent upon localization; those dependent upon meningeal irritation; root symptoms or cauda symptoms or those resulting from a transverse lesion and the systemic degenerations. Pathologically one may differentiate pachy and leptomeningitis chronica fibrosa which may be accompanied by a central softening or changes in other parts of the cord (meningomyelitis). Possibly we may separate spastic paraplegia and postero-lateral sclerosis or rather the clinical picture of these from that of meningomyelitis. Oppenheim and Leyden-Goldscheider contend that both of these clin-

ical pictures are pathologically a meningomyelitis syphilitica. The intermittent claudication of (claudication intermittens de la moelle épinière). Dejerene with exaggerated tendon reflexes and Babinski toe reflexes terminating finally in the clinical picture of spastic paraplegia syphilitica belongs primarily to the vascular form of spinal syphilitic disease. Localized thickening of the dura mater without gummatous formation (pachymeningitis hypertrophica) causing nerve root irritation and compression symptoms is often responsible for indefinite neuralgic pains, hyperesthesias and parasthesias. The so-called Kahler's disease and the progressive muscular atrophies following a spinal root neuritis are all primarily of vascular origin, either of the vessels of the meninges or a perivascular infiltration of the epineurium. Independent syphilitic affection of the peripheral nervous system is also observed and not infrequently isolated nerves are involved. This is particularly true of the cranial nerves (facial and trigeminus). So in trifacial neuralgia or in other localized neuralgias it is of utmost importance to eliminate syphilis before any medical treatment is begun and certainly before operative interference is advised.

Since we know that the spirochaeta is still active in both tabes and paresis the theory of parasyphilitic or metasyphilitic disease is no longer correct and both of these conditions, no doubt, will soon find their places under the head of syphilis of the nervous system.

Probably the most important and the most frequent symptom of syphilitic disease of the nervous system is the loss of the pupillary light reflex; it is almost invariably due to syphilis of the nervous system (celliospinal ganglion). The slightest inequality of size or reaction of the pupils should always arouse our suspicion of syphilis of the nervous system. Even though the Wassermann test on the blood and spinal fluid is negative, it is fairly good evidence that the patient has gone through a syphilitic infection some time. I have frequently seen inequality in the size of the pupils in pulmonary tuberculosis or tuberculous meningitis, but in my opinion loss of the pupillary light reflex does not occur in nonsyphilitic brain tumors. In Ziehen's clinic in the Charité hospital of Berlin all cases of arteriosclerosis with loss of pupillary light reflex and all chronic alcoholics with the same symptom gave a positive Wassermann test on the blood or spinal fluid. E. Forster states that he has never observed the Argyll-Robinson pupil in cases of alcoholism even though the Korsakoff symptom complex was evident without a positive Wassermann reaction.

In 1858 consecutive cases of various nervous disorders admitted in the Neurological Clinic of the University Hospital (Dr. Camp's service) there were 160 cases in which the Wassermann

test on the blood or spinal fluid or on both was positive, showing a marked increase in the percentage when compared with the above statistics where the Wassermann test was not in use. These cases are tabulated as follows:

Nervous Disease	Total No.	Wassermann test. Blood	Spinal Fluid
Tabes	50	29+	50+
Taboparesis	4	3+	4+
General paralysis	21	15+	21+
Cerebrospinal syphilis	17	12+	17+
Meningoencephalomyelitis			
Endarteritis and			
Periarteritis gummosa			
Cerebral syphilis	23	17+	33+
Meningoencephalitis			
Endarteritis and			
Periarteritis gummosa			
Spinal syphilis	5	2+	5+
Meningomyelitis			
Myelitis and			
Periarteritis gummosa			
Brain tumor	3	3—	3+
Hydrocephalus cong	1	+	+
Spinal tumor	2	1+	2+
Syringomyelia	1	+	+
Spastic paraplegia	4	1+	3+
Traumatic myelitis	1	1+	1+
Hematomyelia	1	+	+
Facial palsy	1	+	—
Trifacial neuralgia	6	6+	—
Multiple neuritis	3	3+	—
Meralgia paresthetica	1	—	+
Neuro-fibromatosis	1	+	—
Imbecility	1	—	+
Epilepsy	3	3+	—
Migraine	2	2+	—
Hysteria	4	4+	2+
Neurasthenia	2	2—	2+
Psychasthenia	2	2—	2+
Traumatic neurosis	1	—	+
Muscular atrophy	1	+	+
Paralysis agitans	1	—	—

(with neosalvarsan)
(marked improvement)

A number of cases which came under the writer's observation may be of interest in connection with the above tabulated group. A young woman, 25 years of age, with a negative family and personal history presented herself for treatment of a condition which she said she knew is general paralysis of the insane. The patient in question was a highly intelligent woman and related that beginning with her tenth year she was impressed with the idea that some day she would lose her mind. The idea had persisted until three years ago when it became more definitely formulated in that the form of mental disturbance would be general paralysis of the insane. She also had a fear that her children would have the same disease.

In this case the neurological and psychological, as well as the general physical examination was entirely negative and the diagnosis of psychasthenia was established with a guarded prognosis. The patient insisted that this diagnosis was wrong and persisted in her belief that she would soon lose her mind, the result of paresis. From previous experience I have learned not to disregard a patient's opinion of her own condition entirely and proceeded to make a Wassermann test on the blood and obtained some spinal fluid for examination. The blood was xx positive. The spinal fluid gave a positive Wassermann reaction and a cell count of 125 per cem. The patient was treated accordingly and made a prompt recovery. By this I mean the obsession disappeared and the Wassermann test on the blood and spinal fluid became negative. Another patient threatened to commit suicide the moment the first symptom of approaching insanity appeared which she suspected. She was a woman of 30 years of age and otherwise normal save for the idea of insanity which would come to her sooner or later. There was no reason to suspect syphilis either from the history or from personal observation, but following the same rule as in the preceding case the blood and spinal fluid were examined and both gave a positive Wassermann test. The patient recovered under the proper treatment. A third patient presenting the symptom complex of hysteria, a case of long standing and unsuccessful treatment. The history of the case was not unusual there was no evidence of syphilitic infection. While I always hesitate to do a lumbar puncture in cases of hysteria, I ventured to do so here and the spinal fluid gave a positive Wassermann test; the blood was negative. Treating both the hysteria and luetic infection the patient made a good recovery. Three cases of neurasthenia of long standing with negative histories made good recoveries after the luetic infection was recognized by laboratory tests and the proper treatment applied.

In view of the foregoing illustrations one becomes aware of great difficulties in the differential diagnosis. Of course we determine the existence or non-existence of a syphilitic infection through the history, Wassermann test, etc. Nevertheless, one must refrain from associating in every case the nervous disease with the syphilis and take the symptoms as manifestations of the luetic infection. It is self-evident that with the frequency of syphilis a patient suffering from hysteria, neurasthenia, multiple sclerosis, etc. may formerly have had syphilis. Not only this, but as Virchow emphasized there is a predisposition in the neurosis itself based on a locus minoris resistantiae. On the other hand, the syphilitic infection may have its effect upon the nervous system in reducing the resistance and prevent recovery from the nervous disease.

In the same manner may a trauma precipitate a latent cerebral syphilis which might easily for a time remain concealed under the symptom complex of a traumatic neurosis.

The diagnostic value of the examination of the spinal fluid in syphilis of the nervous system is dependent upon cytological, chemical and biological changes. The cytological change is most marked in the greater number of lymphocytes. While there are also other cells; large mononuclear cells and endothelial cells or possibly genuine plasma cells, besides polynuclear cells in greater or lesser numbers, eosinophiles and red blood cells, the normal spinal fluid is comparatively free from cellular elements. In cerebrospinal syphilis there is an increased number but not to such an extent as one finds them in paresis or tabes. The polynuclear cells are significant of an exacerbation of a chronic meningitis or an acute process. It is needless to say that a lymphocytosis is not significant of syphilis and may occur under various other conditions of the central nervous system but usually not so constant or so marked as in tabes or paresis.

In the chemical examination it is principally a question of determining the albumen content. An increased globulin reaction (Nonne-Apelt phase I) corresponds with an increased albumen content (Nonne-Apelt phase II).

Increased globulin has been found only in organic disease of the nervous system. Nonne found it increased in 96 per cent. of the cases of syphilis of the central nervous system, while in 20 per cent. of secondary syphilis and 42 per cent. of tertiary in which there were no manifestations of syphilis of the nervous system. In the so-called metasyphilitic disease an increase in the globulin is constant. The method of Noguchi has no practical diagnostic value.

In the biological examination of the spinal fluid in syphilis of the central nervous system it is a question of a positive or negative Wassermann reaction, with 0.4-0.8 cem. of spinal fluid it is almost invariably positive in syphilitic disease of the nervous system, while with 0.2 cem. this reaction is less constant in cerebrospinal syphilis than in paresis. In syphilis without manifestations of syphilitic nervous disease the Wassermann reaction on the spinal fluid is constantly negative according to the observations of Boas, Hauptman and Holzmann.

The positive Wassermann reaction is as a rule present in the sixth week after the syphilitic infection. In the secondary period it fails in about 10 per cent., although some authorities claim 99 per cent. positive Wassermann reaction in the secondary stage. In the tertiary period from 70 to 80 per cent. give a positive reaction. The figures are practically the same in syphilis of the nervous system, however, in my own observations there have been a great

many cases of tabes giving a negative Wassermann reaction of the blood and more often than in general paralysis.

There is still a great difference of opinion as to the most valuable therapeutic measure in syphilitic disease of the central nervous system. It is generally believed that the usual methods applied in treating syphilis are inactive in syphilis of the nervous system and various methods for interspinal medication have been suggested. Personally, I have seen some remarkable results in cerebrospinal syphilis, as well as in tabes with subcutaneous and intravenous medication systematically carried out. On the other hand, there have been some drastic results from interspinal injection. The intradural injection of salvarsanized serum recently suggested appears to be less dangerous.

A RETROSPECT.*

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If we would know, realize and appreciate the full freedom, the large liberty, and the perfect government growing out of a democracy, we must of necessity go back over the historic ground of the past; we must mingle with the founders of our country; we must wander through the various scenes and partake, in some degree at least, from Imagination's Casket, the privations, the sufferings, and the hardships of the "First Settlers." And when all this has been done we must cross the broad Atlantic to the home of feudalism and there follow the well-nigh imperceptible thread back, and back, until we find ourselves groping in the gray dawn of the unknown. And so it is in studying the advancement made in this noble profession of ours. Surgery, together with all its allied and related branches, seems to us today so matter of fact, so simple and self-evident in all of its details, that we are apt to take it as an undeniable fact that this bacteriological perfection, which is the common knowledge of us all, has always existed; but not so. If we would know, realize and appreciate the perfect technic of today we must go back over the path trod by our predecessors.

In no department can this be more truthfully said than in obstetrics. The very common sense and matter of fact precautions practiced today in this branch of medicine is one so axiomatic to the average mind that we are oftentimes in danger of overlooking the struggles, ridicules and acrimonious debates through which the contentions passed before the present perfected state and conditions were attained, and at last became the accepted dictum and belief of the entire medical profession.

*Read before the Houghton County Medical Society.

Would we know, realize and appreciate what this means, and has meant, to the world of mothers of the past and future we must let our memories and imaginations have full sway as they sweep over the vast field of suffering, invalidism and death previous to the adoption of anti-septicism and asepticism in the general practice of obstetrics.

More than half a century has rolled away since the memorable Friday evening in Boston when our own Oliver Wendell Holmes presented his epoch-making paper on the "Contagiousness of Puerperal Fever." Truly it was an immortal essay. He startled his hearers with the sentence, "The time has come when the existence of a private pestilence in the sphere of a single physician should be looked upon, not as a misfortune, but a *crime*." This, gentlemen, was five years before Semmelweis, a young assistant working in the maternity at Vienna, was laughed to scorn and to the mad house because he persistently held that every case of puerperal fever was caused by the absorption of putrid animal material.

These two contentions of Holmes and Semmelweis, standing side by side, marked the heavens with the "first steps of day." It was the beginning of the gray dawn of the morning that was breaking in upon suffering humanity, and which was destined to unfold unto the bright, clear light of a grand and glorious day. We know today that puerperal fever is puerperal infection; we know how to prevent it, and we cannot, by any modern sophistry, shift the responsibility.

Those of you who have the Fourth Edition of Playfair, issued in 1882, will find that while he included all puerperal fevers under the head of puerperal septicemia he nevertheless admits that "There were facts difficult to reconcile with theory and for which we were unable to give a satisfactory explanation." In the year 1883, Thomas More Madden, speaking before the British Medical Association, said that "it did not matter by what term or terms we distinguished the malady, provided we recognized that there was a specific infectious disease consequent on parturition." Kindead, Professor of Obstetrics in the University of Dublin, taught that "such fever, from whatever sources arising, except septicemia, is a specific infectious disease, and like those diseases, occurs sporadically and epidemically."

It was during the winter of 1883 and 1884 that puerperal fever was brought up prominently before the profession of America by being thoroughly discussed by the New York Academy of Medicine in December of 1883. It was at this meeting that Thomas defined puerperal fever as 'an infectious disease due, as a rule, to septic inoculation of wounds of the genital tract.' It was at the next meeting that For-

dyce Barker, that grand and commanding figure in American medicine, took part in the general discussion; but unlike Polk and Thomas, who had turned their faces toward the rising sun, Barker saw it sinking slowly in the west and beheld only the dying day. He clung to the old dogma of a specific infectious disease and ridiculed the advanced ideas of his colleagues as follows: "Does every parturient woman in performing the function of maternity, like the scorpion that carries in its tail an agent for suicide if death be threatened by fire, generate an equally fatal poison in a corresponding locality? If so, then the state should make child bearing a penal offense for families who do not have means enough to carry out elaborate antiseptic requirements." While, perhaps, a majority of the profession held that puerperal fever was a septic poison, no one seemed to have a very clear or definite idea as to the nature of the poison. Carbolic acid had been used as a disinfectant in the Copenhagen Maternity since 1870 as it had also been by many obstetricians.

But the time was ripe to put away the time-worn dogmas—to bury forever in the grave of the historic past the ancient conceptions of the causative factor of the slayer of mothers, and the despoiler of homes, and in its place to establish the life-saving gospel of surgical cleanliness. The first demonstrable crusade was inaugurated in the New York Maternity. The mortality in this hospital in 1881 was 2.36% and was thought to be exceedingly low. In 1882 it was 3.25%. During the year 1883 out of 345 parturient women 30 had died, and the morbidity was something enormous. Toward the end of this year the mortality had so greatly increased that one woman in four delivered died.

It was in October of this year that radical and systematic changes were made in this maternity. To no man in this country is more honor due than to Dr. Henry Garrigues, of New York. When he assumed charge of the New York Maternity in the fall of 1885, he brought to the service the fullness and enthusiasm of maturity, together with the thoughtful, calm and energetic doggedness that always marks a man as being one that is and will be superior to the emergency. He laid down principles broad in their comprehension, far reaching in their influence, and which were to be brilliant in their achievement. Sulphur was freely used for fumigation; soap and water followed by the application of a strong solution of bichloride was the menstrum with which the floors and walls received new baptism of asepsism, and in order that the new baptism might become efficacious and entirely supplant the old, the floors of the ward were sprinkled several times a day with bichloride solution. Visitors were

not allowed to visit the wards; the attendants were not permitted to visit other hospitals nor to enter the dead-house. Each patient on entering received a bath and clean linen. The abdomen was washed with soap and water, as was also the genitals, followed in the later by bichloride. The vaginal douche was used in every case, using about two quarts of the bichloride solution. No vaginal examinations were permitted except, mark you, until after the hands had been scrubbed with soap and water with a good brush and then soaked in 1/1000 bichloride. As soon as the head appeared at the vulva a piece of gauze soaked in the bichloride solution was applied to the parts. As soon as the child was delivered the parts were covered as before. The placenta was not ruthlessly torn from its attachment but gently expressed by the Credé method. If the fingers had been introduced into the vagina or uterus then it was followed by the douche but not otherwise. Only those of us who were either in active practice or were students at that time, know of the scepticism and ridicule with which this treatment was received. We all know what its influence was; how the pestilence, together with all its dread, was driven out never to return. How, in three months after the introduction of this treatment, or rather the adoption of these preventive measures, Dr. Garrigues could write: "The effect of this treatment has been wonderful. As if by magic all trouble disappeared. Ninety-seven women have been delivered since its introduction and not only has none of them died, but there has scarcely been any disease among them—only three have had any rise of temperature. The pavillions are scarcely recognizable. Where we used to have offensive odors, feverish, prostrated or despairing patients, over-worked nurses and despondent doctors, the air is pure, the patients look well, their temperatures are normal, the nurses are cheerful and the doctors happy." Gentlemen, in the full light of these facts, and experiences, what general leading his armies over the bloody battlefield to the victorious heights beyond has contributed to the world's progress and happiness more than have those men who defied scorn and ridicule that they might bring joy, happiness and life itself to the homes of humanity. Surely, "Peace hath its victories far more than War," and while the honors and emoluments of this world come to our profession very tardily if at all, yet we know that somewhere in the great unknown future, we shall receive our reward.

"For tho' from out our bourne of Time and Place
The flood may bear us far,
We hope to see our Pilot face to face,
When we have crossed the bar."

TONSILITIS.

JOHN J. REYCRAFT, M.D.
PETOSKEY, MICH.

Someone, I believe at the last meeting, stated, after we had agreed to prepare papers, that they would rather have a paper written upon some subject in every day practice, rather than always to have to listen to some high paper on surgery beyond the reach of the average practitioner, so for that reason I have decided to forsake the erstwhile subject of surgery for a milder theme.

For that reason I have taken up the subject of tonsilitis; a subject which is so familiar to us all, yet I fear has been much neglected by the average practitioner, not wilfully, however, but simply from a lack of thought along the line I am about to disclose.

There is no excuse, however, for tonsilitis, if the public were educated as it should be to its removal; but that of course cannot be accomplished successfully, and we ever have this glandular piece of tissue subject to infection, but not to "cold-taking." I make the cold-taking in quotations, because it is a misnomer, there not being such a condition known to medical science. All is infection, and when we eliminate the staphylococci and streptococci, known, and distinguishable microbes, we do not have tonsilitis. Where do we get tonsilitis? Not from the pure cold air, but from contiguousness to one infected.

Tonsilitis is contagious, none deny, and when one in the family becomes infected, we are likely to have the family, and the visiting neighbors in a like condition.

Another thought that follows very closely is the cause of rheumatism, which but a few years since has been acknowledged to be, not a superabundance of uric acid in the system, but a blood poisoning, due to the same two germs that cause tonsilitis.

My attention was called to this fact some twenty years ago when a patient, F. V., who used to keep the old Occidental Hotel in this city, warned me that I must abort his tonsilitis, or he would come down with an attack of acute articular rheumatism. In those days I was sceptical. Knowing the theory promulgated by writers upon the subject of rheumatism, I was slow to be convinced of the truthfulness of his saying. Later, however, I thoroughly acquiesced in his statement as does everyone else who is familiar with the subject. Knowing this, it is not hard for a practitioner to leave the old theory, that peroxide of hydrogen, and listerine

are sufficient to keep out of the system this dread disease when tonsilitis becomes apparent.

Such inefficient remedies, when used together with some coal tar preparation, are not efficient enough to be used in such cases.

If we are to combat this disease, we must abort the tonsilitis and this is done in two ways: either paint the tonsil with a twelve and a half per cent. solution of silver nitrate, or do a tonsilectomy. I prefer the later, but if any of you are timid for any reason whatever, do not fail to use, what you may even whince at doing; dry your tonsil, use a small swab, and go ahead and paint. This is a twelve foot ladder, however, reaching into a twenty-four foot mow, and I am convinced beyond a doubt by having done this operation many times that we cannot afford to allow a tonsil to remain in a diseased condition.

Chloroform your patient every time; seize your infected tonsil with a four pronged mouth toothed forceps, use no tonsilotime, but a sharp pointed, curved scissors, which shoved in between the tonsil and its capsul, and spread, will loosen at least one third of the adherent tonsil. This done, three times, will permit you to pull it forward and snip it off *in toto*. Should you be afraid that you are opening avenues for infection, it is up to you to sear the scar with silver nitrate or carbolic acid.

By following this later method you are keeping out of the system a germ which often enters, causing rheumatism, endocarditis, and a multiple of other diseases, and you have not at the same time done your patient an injury. On the other hand, you have only hastened what you are about to do in a near future anyhow.

Supposing, however, you have been foolish enough to postpone the inevitable and you are confronted with a post-tonsillar abscess, ordinarily called quinsy, a direct resultant of a neglected operation on the tonsil, the thing is not to open the abscess, by some extra-tonsillar route, but go ahead and remove your tonsil *in toto*, which gives you the most desirable drainage you can have and makes it unnecessary to prolong an abscess for a whole week, as the drainage thereby received, eliminates immediately the abscess and all its attendant disadvantages.

Practitioners in medicine cannot always without doing his patient a harm, remain away from surgery, and I am so convinced by my observation and pioneer work in this line that no resulting harm comes from it that I might cry from the housetops to the timid and unsophisticated to come out in the open, like was commanded by Goliath, and "fight with this uncircumcized Philistine."

Case Reports

REPORT OF A CASE OF ELEPHANTIASIS.*

HOWARD C. ROCKWELL, M.D.
DIAMONDALE, MICH.

Mrs. C., widowed, aged 84, born in New York state and moved to Michigan in 1849. Has resided in Eaton County ever since.

Family History.—Father died aged 90—cause unknown. Mother died aged 45—tuberculosis. No history of cancer in family.

Personal Past History.—Had usual childrens' diseases. Never had scarlet fever or typhoid. Never pregnant. Climacteric at age of 50.

Present Trouble.—First noticed onset of present trouble 20 years ago. Began with slight swelling of both legs which at first extended between hips and ankles. The swelling would be intermittent accompanied with pain and slight fever. Five years it continued this way without much noticeable variation. At the end of this period the skin between knee and ankles became extremely sensitive, feverish, red, excoriated, breaking open and discharging a thin colorless fluid which afterward became milky having no odor. The skin immediately below the knees became pigmented, the same being true around the ankles and instep. In this stage it continued over a period of about ten years subsiding and break-



ing out intermittently. Two years ago her legs began to grow decidedly worse. I first saw her last June. She then complained of pain in both legs,

*Read before the Eaton County Medical Society at Charlotte, January 29, 1914.

sharp shooting in character radiating to the hips. Shortness of breath. She had no cough and complained of no palpitation of the heart. Appetite has always been good. Has occasional attacks of vomiting.

Examination.—Shows a rather scant growth of



dark gray hair on head, no cyanosis. Has a marked kyphosis with a short frame and does not walk any. Sits up and sleeps in chair at night. On right side of face she has an epithelioma which has been present for the past five years. No pulsations present in neck. Respiration and lungs normal. Heart not enlarged, no murmur. Palpation of abdomen shows a large inguinal hernia which has been present 15 years. Has never worn truss. Her legs last June measured 25 inches in circumference at largest point, this was measurement of right limb. Left limb measured 18 inches. They were inflamed at this time and covered with a papillomatous warty growth extending over area shown in picture. The right more marked than the left. She complained of rheumatic pain about lumbar region. There was pitting only upon pronounced pressure. The skin was thickened, rough and warty.

At Present Time.—Right limb measures 18 inches in circumference. Left 15 inches. Left leg comparatively smooth. Does not complain so much of pain.

Laboratory Findings.—Blood pressure 140. Blood count did not show anything except a slight eosinophilia. I did not examine for filaria. Urine negative.

Treatment.—Has consisted of strict cleanliness. Washing and dressing with antiseptic and deodorizing solutions. Internally she has been given Tr. Fer. Chlor. m15 t. i. d. over quite a long period of time.

BIBLIOGRAPHY-REFERENCES-COMMENT-DISCUSSION.

A full bibliography is given by Hyde in *Morrow's System of Dermatology* Vol. III p. 451.

McCall Anderson in the *Journal Cutaneous Medicine*, Vol. I. p. 80, records a case in which the calf circumference measured 27 inches.

Almost all of the cases reported in this country are non parasitic.

S. C. Low in the *Journal of Tropical Medicine and Hygiene*, London, March 15, 1911, gives the etiology of elephantiasis.

McCabe, in *Southern Medical Journal* of May, 1911, reports a case of elephantiasis caused by the streptococcus erysipelatosus associated with bacillus prodigiosus.

Keen in his system says:

In a well advanced stage, which may not be reached until ten years have elapsed, the skin is warty, overgrown to such an extent that it is thrown into thick folds, which may overlap one another and the cuticle is piled up in horny plates, suggestive of the designation "Coats of mail." The deep creases collect and conceal the exfoliated epithelium, the secretion of the skin, and quantities of extraneous matter; and the

decomposition of these gives rise to eruption, inflammations, and ulceration, with the attendant discomforts of itching soreness and stench.

DISCUSSION-TREATMENT.

Lanz, of Leipsic, was able to obtain a complete cure in the case of a man of 49 whose right leg had been gradually enlarging in size for five years without pain; the disfigurement and discomfort resulting from the enormous size of entire limb incapacitated the patient at times. Lanz kept the man in bed ten days with limb raised and then incised thigh down to bone and bored into femur at lower middle and upper third. He then cut some narrow strips from the fascia-lata and worked them into the three holes drilled into the bone, his aim being to induce collateral circulation of lymph by opening a passage from the subcutaneous lymphatics into the intramuscular subperiosteal and marrow network of lymph vessels. Before suturing he made also a number of openings for drainage through the fascia lata.

The fascia lata is an absolute barrier for the lymph route. He was able to affect an immediate and permanent cure.

PROPAGANDA FOR REFORM.

SAL HEPATICA.—Sal Hepatica, marketed by the Bristol-Myer Co., New York, has been refused recognition by the Council on Pharmacy and Chemistry because its composition is secret, because it is advertised indirectly to the public for the treatment of diseases, because exaggerated and unwarranted claims are made for its therapeutic qualities and because its name fails to indicate its chief constituents, but does suggest its use in liver disorders. The Council authorized publication of its report because the exploitation of Sal Hepatica is an important illustration of the way in which physicians are being made parties to the introduction to the public of a patent medicine the indiscriminate use of which must often have resulted in harm, direct or indirect (*Jour. A.M.A.*, Feb. 7, 1914, p. 472).

ORRIN ROBERTSON AND HIS SEVEN SACRED OILS.—Roberson is a quack at present located at Arkansas City, Kansas, who claims to remove gall-stones by means of "Seven Sacred Oils which grow in seven different climes." For the oil he claims "One oil acts specifically upon the entire head and throat. One oil acts directly upon the esophagus. One oil acts directly upon the stomach." And so it goes, each oil acting a little lower down, until we reach the seventh oil which "acts directly" on the rectum. Robertson also exploits a cure for cancer. (*Jour. A.M.A.*, Feb. 7, 1914, p. 473).

MU-COL.—"Mu-col for Cleansing Mucous Membranes" is a nostrum put out by the Mu-col Company, (Inc.), Buffalo, N. Y. The following claims are made: "Mu-col obtains most gratifying results in catarrhal inflammations of the mucous membranes. Leucorrhoea, Tonsillitis, Sore Throat, Cystitis, Internal Hemorrhoids, Nasal Catarrh and Pus Cases respond at once to irrigations with Mu-col solution. Strong solutions of Mu-col have proven of sterling

value in treating Hives, Prickly Heat, Ivy Poison, Sunburn, Eczema, Typhoid and Scarlet Fever." Examination in the A.M.A. Chemical Laboratory showed Mu-col to be a mixture of sodium chlorid and borax, equal parts, with the addition of a small amount of aromatic substances (*Jour. A.M.A.*, Feb. 7, 1914, p. 474).

PIORKOWSKI LABORATORIES NOT LICENSED.—The Public Health Service announces that statements which seem to emanate from the so-called Piorkowski Laboratories in various parts of the country to the effect that these laboratories have been licensed by the U. S. Public Health service are incorrect. Instead, after inspection, a license has been refused the Piorkowski Laboratories of Berlin, Germany (*Jour. A.M.A.*, Feb. 14, 1914, p. 553).

HEX-A--LITH.—Hex-a-lith put out by the Smith-Dorsey Co., Lincoln, Neb. is said to be a combination of hexymethylenamin and lithium citrate. As lithium citrate has a tendency to render the urine alkaline and since hexamethylenamin acts only in an acid medium, the constituents of this preparation are physiologically incompatible (*Jour. A.M.A.*, Feb. 14, 1914, p. 555).

ADMINISTRATION OF LECITHIN.—It has been shown many times that phosphorus in the form of organic compounds as it occurs in milk or in eggs probably changes in the body to phosphate and is subsequently elaborated into lecithin. In view of this there would seem to be no physiologic or biologic reason for preferring isolated lecithin as a medicament to milk or eggs. If it is believed that lecithin is indicated, the administration of one or two raw, or even cooked, yolks of eggs will supply all the lecithin that could be metabolized and presents it in a better manner than an artificial preparation (*Jour. A.M.A.*, Feb. 21, 1914, p. 615).

TRANSACTIONS

OF THE

Clinical Society of the University of Michigan

Stated Meeting, February 13, 1914

The President, R. BISHOP CANFIELD, M.D., in the Chair

Reported by REUBEN PETERSON, M.D., Secretary

HOW BACTERIA CAUSE DISEASE.*

VICTOR C. VAUGHAN, M.D.

(From the Hygienic Laboratory, University of Michigan).

For about fifteen years my students and I have directed our attention and energy largely to the study of the chemistry of bacteria. This work has been collected, systematized and published in book form.* Early in our work we realized that in order to obtain enough cell substance in a pure state to enable us to study successfully its chemistry it would be necessary to devise some method for the growth of massive cultures. After several attempts we succeeded in perfecting the large copper double tanks which have proved wholly satisfactory and have supplied abundant growths, easily obtainable and free from contamination. A copper tank ten feet long, two feet wide, and four inches deep, with a trough around the edge one inch deep, has a cover which, when lowered into place, rests in the trough. This tank is supported by an iron frame of gas piping, the legs of which rest on rollers, so that the whole may be easily moved about the room. An inner tank, two inches shorter and two inches narrower, also provided with a trough that runs around the edge, sits in the large one, and is supported two inches from the bottom of the larger one by iron cross-bars. The bottom of the outer tank and the seal trough on the edges are filled with water. The seal trough of the inner tank is filled with glycerin. Both lids are raised and lowered by wire ropes passed through pulleys fixed in the ceiling. The iron frame supporting the tanks may be of any desired height. In our incubating room we have a nest of six tanks, three of which are on frames four feet high and three on frames two feet high. This economizes space, as the lower ones

can be rolled under the higher ones. Both lids are supplied with vent tubes which are plugged with cotton in sterilization. Twenty liters of three per cent. agar is placed in the inner tank; both lids are lowered into their respective troughs, and with large gas burners at full blast underneath, the apparatus is a sterilizer. After three sterilizations on successive days the medium is inoculated by pouring a liquid culture through the vent tubes in the lid of the inner tank. Then with upper lid lowered into the water trough and gentle heat, which may be controlled by a thermoregulator, it becomes an incubator. With a number of tanks in a small room it is better to heat the room to the desired temperature, thus regulating the heat, than it is to heat each tank separately. (A photograph of this tank is shown in Figure 1).

After removal from the tanks the bacterial cellular substance may be washed with various fluids. As a rule, we have washed once or twice with sterile salt solution by decantation and then repeatedly with alcohol, beginning with 50 per cent. and increasing to 95 per cent. The substance is then placed in large soxhlets and extracted first for one or two days with absolute alcohol and then for three or four days with ether. These extractions with alcohol and ether should be thorough, in order to remove all traces of fats and waxes.

After extraction, the cellular substance is ground, first in porcelain, then in agate mortars, and passed through the finest meshed sieves. If there be bits of agar in the bacterial cellular substance, which is seldom the case, it is separated by the sieve and discarded. The one who grinds the cellular substance should wear a mask in order to protect himself; notwithstanding this precaution, several workers have been acutely poisoned, especially with the typhoid bacillus. Of course, there is no danger of infection, as the material, after the treatment already described, contains no living bacilli. The finely

*Protein Split Products in Relation to Immunity and Disease. Lea & Febiger. Philadelphia, Pa., 1913.

ground cellular substance in the form of an impalpable powder may be kept in wide-mouthed bottles in a dark place, and if so kept it retains its toxicity for years, but when long exposed to the light, even if kept perfectly dry, it becomes less poisonous.

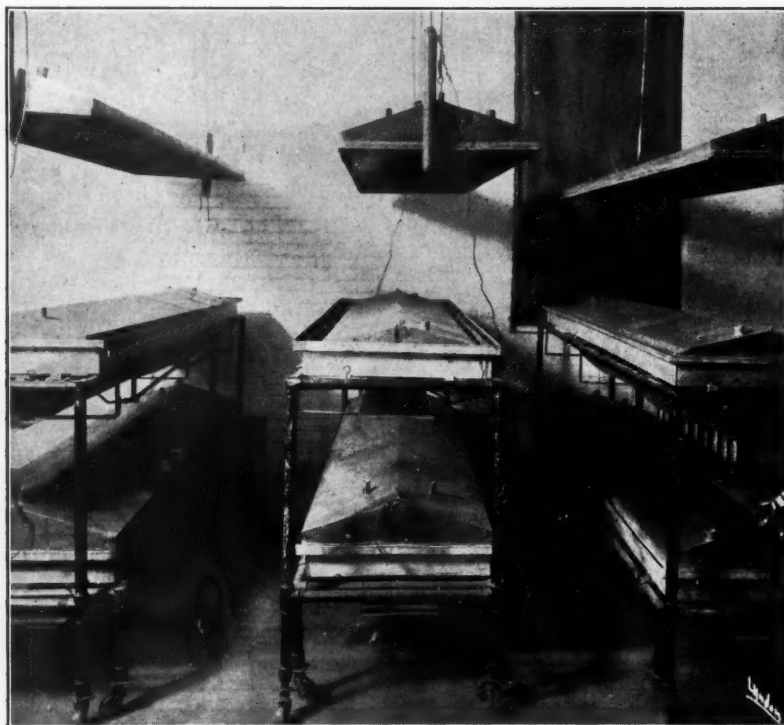
With an abundance of bacterial cellular substance obtained from the tanks the following facts were established for the colon bacillus.

1. The poison is contained within the bacterial cell from which it does not, at least under ordinary conditions, diffuse into the culture medium.

2. The poison is not extracted from the bacterial cell by dilute salt solution, alcohol, or eth-

7. The bacterial cellular proteins are, so far as their toxicity is concerned, quite resistant to the action of pepsin and trypsin.

More thorough study of the bacterial cellular substances demonstrated the fact that the bacterial cell consists largely of complex proteins. It has been assumed that bacteria are low forms of vegetable life; our work, which has been confirmed recently in Kossel's laboratory, shows that this is not true and that bacteria, although simple morphologically, are highly complex chemically, in fact, bacteria are as complex chemically as the cells of our own bodies. This is a most important fact inasmuch as it shows that the bacterial cell and the body cell are much



The incubating room, lids raised.

er, at ordinary temperature or at the boiling point of these fluids.

3. The cellular substance of the colon bacillus may be heated with water without destruction of its poisonous group.

4. 0.5 per cent. solutions of the caustic alkalies disrupt the cellular substances of the colon bacillus slowly and imperfectly.

5. Boiling with a 0.2 per cent. dilution of hydrochloric acid has but little effect upon the bacterial cell or its contained poison.

6. Heating the cellular substance for an hour in an open dish on the water-bath, with from one to five per cent. hydrochloric acid, breaks up the cells and does not wholly destroy the toxicity of the cell content; however, prolonged boiling with one per cent. or stronger dilutions of hydrochloric acid does destroy the poison.

alike in chemical composition and, as we later demonstrated, that different kinds of bacteria differ in chemical composition. Bacteria are particulate proteins containing, at least two carbohydrate groups, a nuclein group and one or more protein groups; consequently when bacteria cells are disrupted they supply carbohydrates, nuclein bodies and amino acids.

After many failures we succeeded in splitting up bacterial cellular substances into poisonous and non-poisonous portions. We were able to do this not only with pathogenic but with non-pathogenic bacteria. Having found that bacterial cellular substances contain a highly active poison the question arose as to whether or not other proteins, bacterial, vegetable, and animal contain poisonous groups; moreover, we demonstrated that the poison obtained from all

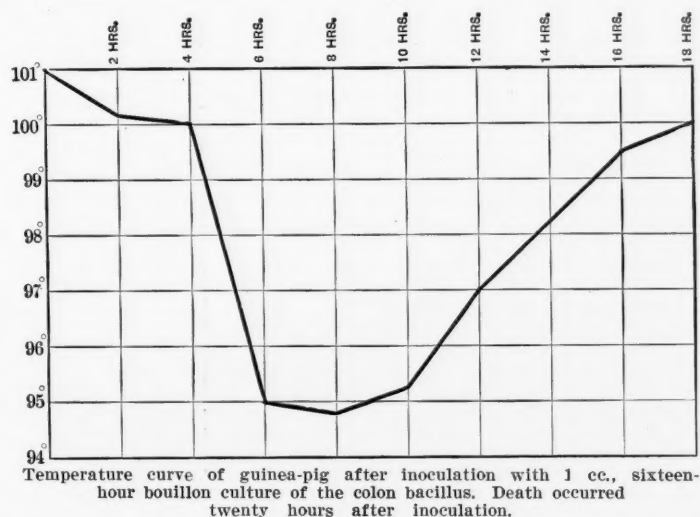
these varieties of proteins has the same, or at least similar, action. Egg-white contains just as much poison and the same poison practically as that found in the tubercle bacillus.

A comparison of the effects of the living bacillus, the dead cellular substance, and the free poison is of great interest and throws much light on the phenomena of infection.

When a guinea-pig is inoculated with a fatal dose of the living colon bacterium, practically no symptoms whatever are noticeable for a period varying from six to twelve hours, according to the size of the dose given. This may be considered as the period of incubation and is roughly proportional to the amount of living culture injected. This period of incubation represents the time taken for the bacillus to multiply and to be destroyed to such an extent that sufficient poison may be liberated through its disintegration to produce recognizable effects in the ani-

by rigidity and spasms of the abdominal muscles on pressure. At autopsy, the only gross lesion present is a marked hemorrhagic peritonitis with a large amount of bloody fluid in the cavity.

On the injection of a fatal dose of the dead cellular substance intraperitoneally, the length of the period of incubation is shortened, in fact, we have cut out one of the processes of incubation, that is, the growth of the bacillus in the body, the bacillus has been grown artificially and enough of it has been injected into the animal to cause its death. Under ordinary conditions the period of incubation is determined by the length of time necessary for the body cells to disrupt the bacterial substance sufficiently to set free enough of the poison to produce recognizable effects. In the case of the guinea-pig treated with dead substance of the colon bacillus this period is reached in about four hours; at the end of this time the temperature begins to fall and there



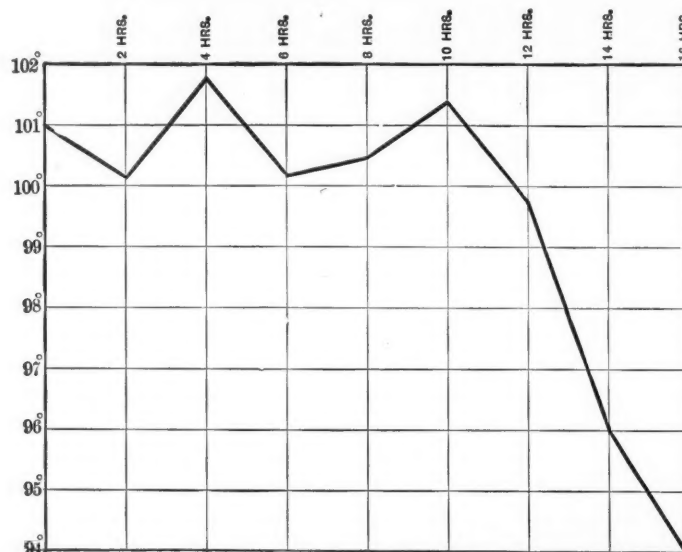
mal. This period of incubation is in reality the crisis of the disease and the outcome depends on whether all bacteria have been destroyed before a fatal dose of the poison is set free. It is during this period that individual resistance and acquired immunity are important factors acting by causing increased destruction of bacilli before a fatal dose is set free. During this time the temperature of the animal may rise to a greater or less extent or may remain stationary; the animal is active and is in no way distinguishable from its untreated fellows. At the end of the period of incubation the animal becomes less active, it hangs its head, and apparently enters into a state of stupor; at the same time the temperature begins to fall abruptly, as can be seen by Fig. 2. The temperature will often fall from 101° to 94° F. or even lower within from two to four hours, and this fall is progressive and continues until the animal's death, immediately preceding which a temperature as low as 85° F. is not uncommon. At the same time the animal shows signs of peritonitis, as is evidenced

by a decided drop until time of death, provided the dose given is a fatal one. If a non-fatal dose has been injected the temperature, as will be seen from Fig. 3, has reached the minimum at the end of from six to eight hours and has returned to normal in from twelve to twenty hours. Accompanying the fall in temperature there is apparent lassitude, stupor and roughing of the coat. In cases in which many times the fatal dose has been given, the animals occasionally die within from four to six hours with convulsions, a feature which can now and then be observed after injection of large quantities of old living cultures. At autopsy we find a picture similar in all respects to that following inoculation with living bacillus. There is a marked hemorrhagic peritonitis, the peritoneal cavity containing bloody fluid, together with unabsorbed bacterial cell substance. From this we see that practically the sole difference between the effects following inoculation with the living bacillus and the injection of the dead bacterial substance is the shortening of the period of incubation due, no

doubt, to the fact that the poison is liberated much more rapidly and in greater concentration in the second case. Since dead bacteria, both pathogenic and non-pathogenic, will kill animals when injected into the peritoneal cavity in sufficient amount it must be evident that the effects are not due directly to the growth of bacteria in the body; it must also be evident that whether a given bacillus is pathogenic or not does not depend upon its capability of forming a poison but upon its capability of growing and multiplying in the animal body.

When the free poison is given the temperature begins to fall within five to fifteen minutes and often it will be found to have reached 94° F. and even lower in many instances, (See Fig. 5). At first, after an interval of from five to ten minutes immediately following the injection, the animal appears restless, runs about the cage,

until all the muscles of the body become involved in violent clonic convulsions. This stage, when present, presages a fatal outcome; rarely an animal recovers after reaching the convulsive stage. During a convulsion, or occasionally in the interval of calm, respiration ceases. The heart, however, continues to beat, at first with perfect regularity and no acceleration; indeed, the rate seems to be somewhat slower than normal. Gradually the beat becomes more and more feeble, the rate and regularity being preserved to the end. It is usually only after an interval of from three to four minutes after the cessation of respiration that the heart ceases to beat. As has been previously stated, a fatal issue, if it occurs at all, always results within one hour after injection and usually within from thirty to forty minutes. This is to a large extent independent of whether the dose is the



Temperature curve of guinea-pig after intraperitoneal injection of non-fatal dose of crude bacterial cell substance.

and shows a great tendency to scratch itself, this undoubtedly being due to itching sensations in the skin caused by irritation of peripheral nerves. The animal then begins to show evidence of lack of co-ordination, which is rapidly followed by partial paralysis, which is especially marked in the hind extremities. This stage lasts for from five to ten minutes, during the latter part of which the animal usually lies quietly on one side. From this state the animal passes into what one might term the convulsive stage. These convulsions are usually clonic in nature and, as a rule, at first involve only the neck muscles, the head being momentarily drawn backward on the back. At first these convulsions are but slight in degree and are separated by considerable intervals of time. Soon, however, they become much more frequent and of much greater severity. Gradually they become more and more general in their extent.

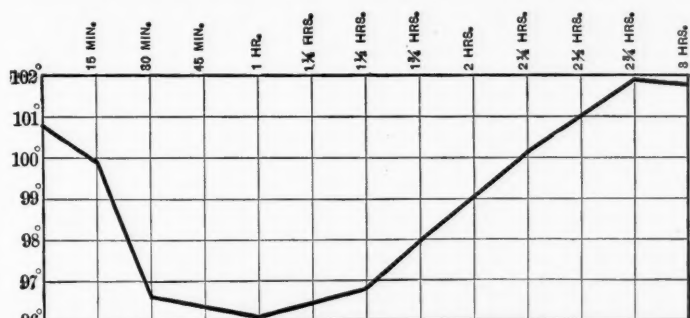
minimum lethal one or two or three times that amount. It is certainly entirely independent of the size of the pig. Death, of course, results at slightly different times with different batches of the poison, but even in this case the interval of time between injection and a fatal issue does not vary to any great extent. A dose which has proved to be the minimum fatal dose for one pig will almost surely prove to be the same for another. In other words, we have done away entirely with the period of incubation, and the poison acts so rapidly that individual resistance plays no part; hence, the animal acts almost with the exactitude of a chemical compound into which for all practical purposes it has been converted. The period of incubation has ceased to exist since the poison is no longer contained within either the dead or the living bacillus, but is present in a free and uncombined form, capable of uniting immediately with those body

cells for which it may possess a special affinity.

After the above described work had been done, the phenomena of protein sensitization or so-called anaphylaxis became prominent and it will be necessary to discuss the elements of this discovery.

The older medical literature occasionally records facts which in the light of more recent and extended knowledge are known as the phenomena of protein sensitization. Such were some of the experiences recorded in the early attempts at the transfusion of blood. Many of the untoward results reached in the procedure and beyond the ken of that time are now fully explained. Behring and Kitashima¹ found on immunizing an animal to tetanus toxin that it died in convulsions notwithstanding the fact that the blood serum was richly charged with antitoxin. They explained this by assuming the existence of a condition of "hypersensitiveness" to the toxin. With our present knowledge we see no reason for ascribing this to the toxin. There is, so far as we know, no evidence that

tained a soluble poison which he named synzytiotoxin. Later, he showed that hay fever results from the parenteral digestion of the proteins of pollen. Both of these points will be discussed in more detail later. Wolff-Eisner⁵ discussed the theory of endotoxins and their application to various diseased conditions, in a very suggestive manner, but added little to our exact knowledge. Richet⁶ has made many valuable contributions to this subject. In his first report made with Portier in 1902, he worked with an extract from the tentacles of a muscle and showed that an injection of this made the animal much more susceptible to a second one. Unfortunately, he coined the word anaphylaxis as most suitable to cover this condition of increased susceptibility. He used this word understanding it to mean "without protection," indicating that the first injection destroyed any natural resistance that the animal might possess against the poison. Now, we know that the condition of sensitization is essential to certain forms of immunity, as was first indicated by



Temperature curve of guinea-pig treated with 45 mgs. of the soluble poison intraperitoneally.

animals can be rendered hypersensitive to either toxin or antitoxin. Neither has ever been obtained free from proteins, and since all true proteins, so far as we know, sensitize, there seems no sufficient justification in ascribing a sensitization induced by a protein solution containing a toxin to a latter. Buchner² repeatedly injected bacterial proteins into men and noticed that the cardinal indications of local inflammation, tumor, rubor, dolor, and calor resulted. Furthermore, he noted that fever increased with repeated injections, Krehl and Matthes³ induced fever in animals by repeated injections of albumose and peptone.

Weichardt⁴ made an advanced study in the domain which we now designate as anaphylaxis. He repeatedly treated rabbits with protein expressed from placental cells, and found that some of these died promptly on subsequent injections. Furthermore, he mixed the serum of animals thus treated with placental cells and ob-

Vaughan and Wheeler,⁷ and the inappropriateness of the term anaphylaxis is self-evident. However, the word has come into general use, and with this explanation we will continue it. V. Pirquet⁸ proposed and has continued the use of the word "allergie," meaning altered energy. This is much more suitable, inasmuch as it simply expresses a fact and binds no one to any theory. However, "allergie" has not been usually employed, and we will use "protein sensitization," "hypersensitiveness," "anaphylaxis," and "allergie" as synonyms.

The fact that animals which have once received an injection of protein are liable to sudden death after a second injection of the same kind has been known for many years. Ever since the opening of the Hygienic Laboratory of the University of Michigan (1888), animals once used have been segregated and kept in cages marked "used animals," which indicated that conclusions could not be safely drawn from re-

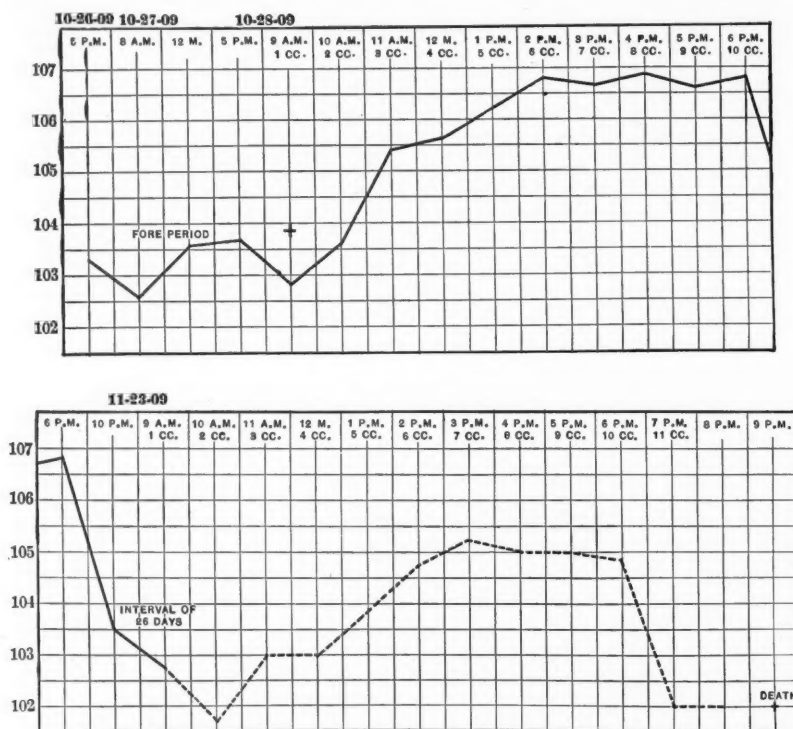
1. Berl. Klin. Woch., 1901, No. 6.
2. Berl. klin. Woch., 1890, 216; Münch. med. Woch., 1891, No. 3.
3. Arch. f. exper. Path. u. Pharm., 1895, 232; *ibid.*, 1896, XXXVI, 437.
4. Berl. klin. Woch., 1903, No. 1.

5. Zentralbl. f. Bakt., 1904, XXXVII; Münch. med. Woch., 1906; Derm. Zentralbl., 1906; Berl. klin. Woch., 1907.
6. Compt. rend. de la Soc. biol., 1902; Ann. de l'Institut Pasteur, 1907, XXI, 497; *ibid.*, 1908, XXIII; *ibid.*, 1909.
7. Jour. Infect. Dis., 1907.
8. Münch. med. Woch., 1906.

sults obtained when these animals were employed a second time. In the standardization of diphtheria antitoxin it soon became evident that the guinea-pig that survives one test could not be relied upon in a second one. In the late nineties, Parke, Davis & Co., large manufacturers of antitoxins, ascertained this fact and offered to supply the Hygienic Laboratory of the University of Michigan with "used" guinea-pigs at a small price. The offer was accepted, but the animals were found dear at any price, as they suddenly and unexplainably died when treated with horse serum.

This condition evidently was observed by others, and Theobald Smith mentioned it to Ehrlich, who set Otto to work to find the ex-

antigen, after a period of incubation becomes hypersensitive to the same or to a closely related substance, and when this condition can be passively transferred to fresh animals by the serum or organ extracts of the sensitized animal." Biedl and Kraus,¹² omitting passive anaphylaxis, give the following: "By anaphylaxis we mean that state of specific hypersensitiveness induced in animals by protein injections, and in which symptoms of poisoning follow subsequent injections of the same protein in doses which would have no effect upon untreated animals." With some explanation to be given later we accept these definitions as quite satisfactory. In the meantime it is desirable to have a clear understanding of the meaning of the terms em-



The production of continued fever in a rabbit by repeated subcutaneous injections of egg-white.

planation. Otto⁹ published his results under the title "Das Theobald Smithsche Phänomen der Serumüberempfindlichkeit." However, simultaneously with these observations on animals used in the standardization of antitoxin, the profession had occasion to observe the effects of injections of antitoxin in human beings. As early as 1903, v. Pirquet¹⁰ wrote concerning certain clinical effects following antitoxin treatment, and in 1905 he and Schick published a monograph "the serum disease," "Die Serumkrankheit."

Friedemann¹¹ offers the following definition: "We speak of anaphylaxis when the organism, in consequence of a previous treatment with an

employed in discussing this subject. The substance which induces the anaphylactic state is generally known as the "antigen." This implies that it gives rise to the production of an antibody, and the selection of this word has been determined by an attempt to correlate the phenomena of anaphylaxis with the theory evolved by Ehrlich in explanation of the production of antitoxins by treatment with toxins. In truth the "antigen" of anaphylaxis is not a toxin, nor is the new substance generated in the body of the treated animal an antitoxin. The term "anaphylactogen" is unobjectionable, since it is applicable to any substance which induces the anaphylactic state. Sensitizer is a good word, and commits one to no theory. The same is

9. V. Leuthold Gedenkschrift, 1906.

10. Wien. klin. Woch.

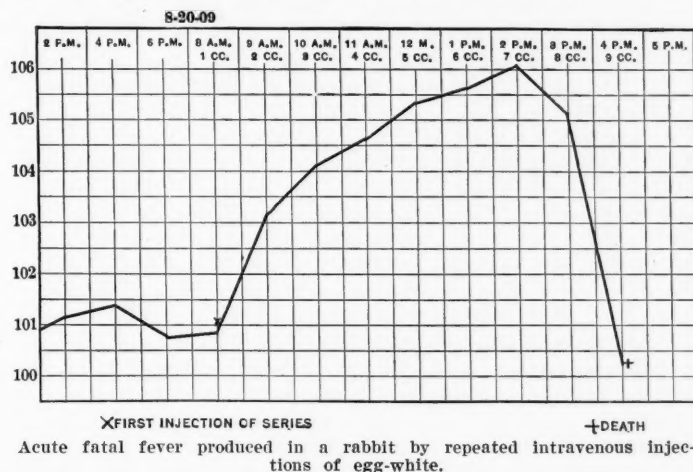
11. Jahresb. u. d. Ergeb. d. Immunitätsforschung, 1910, VI.

12. Kraus and Levaditi's Handbuch d. Technik u. Methodik d. Immunitätsforschung Ergänzungsband.

true of the term "sensibilisinogen" used by our French Confreres. The sensitizer causes the body cells of the treated animal to elaborate a specific proteolytic ferment which digests or splits up the sensitizer. Again, following the nomenclature of Ehrlich, this ferment elaborated as a consequence of the introduction of the sensitizer is generally designated as the "antibody." It would be equally rational to speak of pepsin as an antibody of beefsteak, because the former digests the latter. The theory evolved by Ehrlich in his studies on toxin immunity is the product of a genius of the highest order. It has stimulated research, which has resulted in discoveries of the greatest importance, but the attempt to explain all physiologic and pathologic processes by this theory, and to describe them in the nomenclature of this theory is unscientific. To say that anaphylaxis is the result of protein-antiprotein reaction is to talk jargon. When foreign proteins are taken into the alimentary canal they must be digested before they

foreign protein is introduced into the blood or tissue it stimulates certain body cells to elaborate that specific ferment which will digest that specific protein. When such a protein first comes in contact with the body cells the latter are unprepared to digest the former, but this function is gradually acquired. The protein contained in the first injection is slowly digested, and no ill effects are observable. When subsequent injections of the same protein are made, the cells, prepared by the first injection, pour out the specific ferment more promptly and the effects are determined by the rapidity with which the digestion takes place. The poisonous group in the protein molecule may be set free so rapidly and in amount sufficient to kill the animal. This in brief is an explanation of the phenomena of anaphylaxis.

In 1907 Wheeler and I proposed a theory of sensitization, the principles of which may be stated as follows:



are absorbed. This means that their large molecules must be split into smaller ones, and this must be continued until there are no more protein molecules left. Every protein molecule contains a poisonous group, and in normal, alimentary digestion this group is rendered non-poisonous by further cleavage before absorption takes place. When foreign proteins find their way into the blood and tissues they must be digested. This is accomplished, as it is in the alimentary canal, by proteolytic ferments but the danger from the poisonous group in the protein molecule is evidently greater in parenteral than in enteral digestion. Both enteral and parenteral digestion are physiologic processes. Every living cell has its own proteolytic ferments, otherwise it could not live. When stimulated it pours out this ferment, and it does so only when stimulated. The function of a cell ferment depends upon the kind of cell elaborating it, and to a certain extent upon the stimulating substance. The proteins are the normal stimulants to cell secretion. When a

1. Sensitization consists in developing in the animal a specific proteolytic ferment which acts upon the protein that brings it into existence, and no other.

2. This specific proteolytic ferment stored up in the cells of the animal as a result of the first treatment with the protein remains as a zymogen until activated by the reinjection of the same protein.

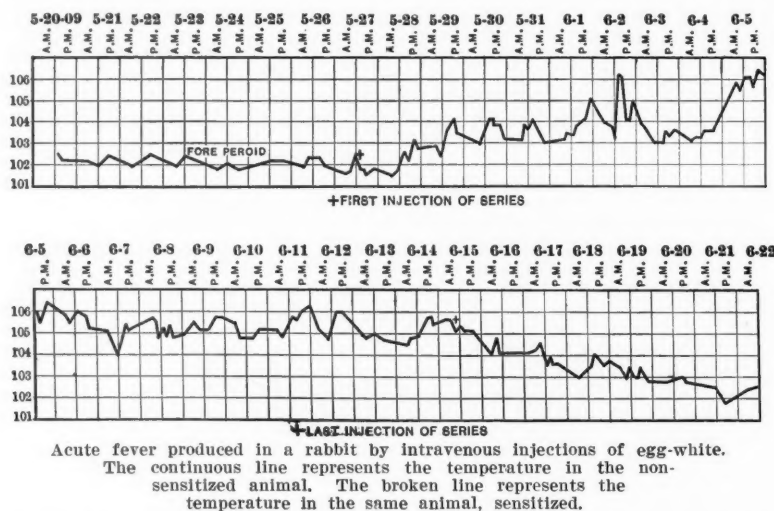
3. Our conception of the development of a specific zymogen supposes a rearrangement of the atomic groups of the protein molecules of certain cells, or an alteration of their molecular structure. In other words, we regard the production of the specific zymogen not as the formation of a new body, but as resulting from an alteration in the atomic arrangement within the protein molecule, and a consequent change in its chemism.

4. Some proteins in developing the specific zymogen produce profound and lasting changes in molecular structure, while the alterations induced by others are slighter and of temporary

duration, the molecular structure soon returning to its original condition.

5. Bacteria and protozoa are living, labile proteins, while egg-white, casein, serum albumin, etc., are stabile proteins. The proteins of one group are in an active, while those of the other are in a resting state, but both are essentially proteins made up of an acid or poisonous chemical nucleus, and basic, non-poisonous groups. Bacterial immunity and protein sensitization, apparently antipodal, are in reality the same, and each consists in developing in the animal body the capability of splitting up specific proteins. If the living protein be split up before it has time to multiply sufficiently to furnish a fatal quantity of the poison, the animal lives and we say it has been immunized. If the stabile protein be introduced into the animal body it leads to the development of a specific proteolytic ferment, and if enough of it to supply a fatal dose be reinjected after this function has been developed, the animal dies.

gether tends to resist this process of disintegration. The pathogenic bacterium assimilates the nutritious constituents of the fluids of the animal body, builds them into its own tissue, converts them into substances foreign to the host, and finally, when the bacterial cell goes to pieces either from spontaneous dissolution, or through the aggressive action of some animal cell, these reconstructed chemical groups are set free and poison the animal, inducing lesions in various tissues, and, in many instances, so interrupting the vital functions as to cause death. It is in harmony with these statements that Friedberger has been able to induce aseptic pneumonia by spraying horse serum into the lungs of guinea-pigs sensitized with the same, and Schittenhelm and Weichard have established "enteritis anaphylactica" by the reinjection of egg-white into sensitized dogs. It is more than probable that cholera infantum and the kindred summer diarrheas result from the absorption of undigested milk and consequent sensitization. The design-



6. We are compelled to change our ideas concerning the causation of the lesions of the infectious diseases. Formerly, we believed the structural changes to be due wholly to the living, growing, feeding microorganisms. For instance, we were sure that the intestinal ulcerations of typhoid fever are caused by the living bacilli. Now we know that these lesions follow the intravenous injection of dead proteins. As has been stated, each foreign protein has its predilection tissue in which it is largely deposited, whose cells it especially sensitizes, and where it is disrupted. This explains the characteristic lesions and symptoms of the different infectious diseases. Bacterial inflammation is essentially a chemical process, or is due to the disruption of cell molecules through the chemical affinity between certain groups in the bacterial cell and certain groups in the cell of the animal. So long as the bacterial cells are alive the chemism that holds the living molecule to-

nation "protein disease" might be used to cover the majority of bacterial and protozoal disease, and many of these hitherto regarded as auto-genous.

7. It seems to be a physiologic law that the specific ferments elaborated by living cells are determined by the proteins brought into contact with them, but as yet we know but little concerning these bodies which we call ferments. That they are labile chemical bodies resulting from intramolecular rearrangement in the protein molecules of the cell seems a plausible theory, but at present it is only a theory. We know but little of the action of these so-called ferments upon their homologous proteins. Our knowledge of the chemistry of protein sensitizers is exceedingly limited, and, as we have pointed out, it is highly desirable that work in this direction should be prosecuted with vigor, because we need sensitizers free from the poisonous group. Furthermore, there is the question

why small doses of protein induce fever while large doses have no such effect. At present we have no satisfactory answer to this question. If it could be conclusively demonstrated that the toxins are ferments, the subject of the etiology of disease would be greatly simplified. We have elsewhere, given our reasons for holding that the toxins are ferments, and at this point we wish to formulate what we believe to be two biologic laws:

(a) When the body cells find themselves in contact with, or permeated by, foreign proteins they tend to elaborate specific ferments which digest and destroy the foreign proteins.

(b) When body cells are attacked by destructive ferments they tend to elaborate anti-ferments, the function of which is to neutralize the ferments and thus protect the cells.

In 1909, Wheeler, Gidley and I demonstrated that any desired form of fever, acute, fatal, continued, intermittent, or remittent can be induced in animals by regulating the size and frequency of the doses of foreign protein administered parenterally, and in 1911 Cumming, Wright and I extended the details of this work. As a result of these studies we reached the following conclusions:

1. Large doses of unbroken protein administered intra-abdominally, subcutaneously, or intravenously have no effect upon the temperature; at least do not cause fever.

2. Small doses, especially when repeated, cause fever, the forms of which may be varied at will by changing the size and the interval of dosage (for fever charts see Figs. 6, 7, and 8).

3. The effect of protein injections on the temperature is more prompt and marked in sensitized than in fresh animals.

4. The intravenous injection of laked blood corpuscles from either man or the rabbit causes in the latter even in very small quantity, either in single or repeated doses, prompt and marked elevation of temperature.

5. Laked corpuscles after removal of the stroma by filtration have a like effect.

6. Protein fever can be continued for weeks by repeated injections, giving a curve which cannot be distinguished from that of typhoid fever.

7. Protein fever is accompanied by increased nitrogen elimination and gradual wasting.

8. Protein fever covers practically all cases of clinical fever.

9. Animals killed by experimentally induced fever may die at the height of the fever, but, as a rule, the temperature rapidly falls before death.

10. Fever induced by repeated injections of bacterial proteins and ending in recovery is followed by immunity.

11. The serum of animals in which pro-

tein fever has been induced digests the homologous protein in vitro.

12. Fever results from the parenteral digestion of proteins.

13. There are two kinds of parenteral proteolytic enzymes, one specific and the other non-specific.

14. The production of the non-specific ferment is easily and quickly stimulated.

15. The development of the specific ferment requires a longer time.

16. Sensitization and lytic immunity are different manifestations of the same process.

17. Foreign proteins, living or dead, formed or in solution, when introduced into the blood soon diffuse through the tissues and sensitize the cells. Different proteins have predilection places in which they are deposited and where they are, in large part at least digested, thus giving rise to the characteristic symptoms and lesions of the different diseases.

18. The subnormal temperature which may occur in the course of a fever or at its termination is due to the rapid liberation of the protein poison, which in small doses causes an elevation, and in larger doses a depression of temperature.

19. Fever *per se* must be regarded as a beneficent phenomenon, inasmuch as it results from a process inaugurated by the body cells for the purpose of ridding the body of foreign substances.

20. The evident sources of excessive heat production in fever are the following: (a) That arising from the unusual activity of the cells supplying the enzyme; (b) That arising from the cleavage of the foreign protein; (c) That arising from the destructive reaction between the split products, from the foreign and the proteins of the body.

From the work already detailed I have formulated statements concerning the phenomena of infection. These may be briefly stated as follows:

In all infections there are two principal factors—one the infecting virus and the other the body cell. In addition to these there is the environment in which the struggle for supremacy between the virus and the body cell takes place. This consists of the unorganized fluids of the body, and is of great weight in determining the result of the contest. In the first place, what do we know of the infecting virus? As we have seen, bacteria are particulate, specific proteins. Since they are particulate, we speak of them as bacterial cells. It is not, however, essential that an infecting virus be participate in the sense that it be possessed of substance and form recognizable to our limited sense of sight even when aided by the most perfect microscope. There are many filterable viruses. Some pass through our finest porcelain filters

and cannot be deposited from the fluids in which they exist even when kept for hours in the most efficient centrifuge manufactured. Theoretically, there is no reason why a virus may not exist in any degree of lability of structure. The bacteria are particulate and solid, which means that their structure is so radically different physically from the medium in which they exist that they can be recognized by sight, aided by proper magnifying lenses, but viruses may be semi or wholly fluid. In such instances their structure is not sufficiently differentiated from the medium that we can recognize them. According to our conception, a living protein does not necessarily possess a form recognizable to our limited sense even when aided by the most perfect lenses.

One of the most important results of our work, in our opinion, is the demonstration that bacteria are chemically not simple, but quite complicated in structure. Morphologically, they show but little or no differentiation in structure, but chemically they are quite as complicated and complex as many of the cells of higher animals. They contain carbohydrates, nuclein bodies, and polymers of the mono- and diamono-acids. They are glyconucleo-proteins. We interpret this as signifying that functionally they are highly developed.

While an infecting virus may be solid, semi-solid, gelatinous, or liquid, we will, in the further consideration of the phenomena of infection, take the particulate type, the bacterium, as an example of an infecting agent.

What are some of the capabilities of a bacterial cell? In the first place it possesses that attribute which distinguishes and characterizes all living matter—the capability of growth and reproduction. In order to grow and multiply its molecular structure must be labile—in a state of constant change. Some bacteria under certain conditions may pass into a resting state characterized by the formation of spores, but these are awakened into life when the environment becomes fit, and the spore develops into the active form when it infects. In all instances the active, infecting agent is a living protein, capable of growth and multiplication. In order to do this it must carry on a constant exchange in matter with the medium in which it exists. It must assimilate and eliminate. It must absorb groups from the molecules about it, and cast out those which it has already used. Stop this process and the continuation of life is impossible. Every living cell, be it bacterial, vegetable, or animal, must feed or cease to exist. Besides, a cell is limited in its food supply by that which lies within its reach. There must, therefore, be a certain supporting relation between the bacterial cell and the medium. The groups derived from the medium must fit into the molecular structure of the cell, otherwise

they would be of no service to it. This necessitates the cleavage of the molecules of the medium along definite lines. Many kinds of cells may live in the same or like media, but for each kind of cell the cleavage of the medium must be specific. From this it follows that the agent by which the cleavage products are secured must be supplied by the cell itself, and must be peculiar to that kind of cell. These cleavage agents which prepare foods for the cell from the medium are known as ferments, and each kind of cell has its own characteristic and specific ferments. As to the real nature of ferments, we know little or nothing, but that every kind of cell has its specific ferment or ferments, we do know. The same ferment may not be able to break up all proteins. In this respect there are great variations in the proteolytic ferments. Some digest a wide variety of proteins while others are capable of acting only on one specific protein. There must be a relation between the ferment and its substrate. As Fisher once said, the former must fit the latter as a key fits into the lock, and as there are master keys that open many doors, so there are general proteolytic ferments, and as there are special keys that fit only one lock, so there are specific proteolytic ferments. It will be observed that we have used the word "specific" in two senses in speaking of proteolytic ferments. Each kind of cell has its specific ferment, and each protein may have its specific ferment. This double use of the term "specific" should be borne in mind, since there seems to be no way to avoid it.

It follows from what has been said that a bacterium placed in a medium in which its ferment is ineffective cannot grow and multiply. A bacterium which cannot grow and multiply in the animal body cannot cause an infection. Its inability to grow and multiply in the animal body may be due to the fact that its ferment or ferments cannot digest or properly break up the proteins of the animal body. This is one of the reasons why the great majority of bacteria are non-pathogenic or are harmless. These organisms when grown on suitable media produce as much poison as the pathogenic bacteria, but not being able to feed upon the proteins of the body they die. This, however, is not the sole, and probably not the most important, cause of the failure of so many varieties of bacteria to do harm to the higher animals. What has been said about the production of ferments by the bacterial cell is equally true of the body cell. In fact, it is true of every living cell. The body cell has its specific ferments, and the bacterial cell being protein substance is liable to be digested by the ferments elaborated by the body cells.

In the inability of the bacterial cell to grow in the animal body either because it cannot feed upon the proteins of the body, or because it is

itself destroyed by the ferments elaborated by the body cells lies the fundamental explanation of all forms of bacterial immunity either natural or acquired. Toxin immunity needs further explanation. Certain bacteria, of which the diphtheria bacillus may be taken as a type, elaborate soluble, extracellular substances known as toxins. These are probably ferments or closely allied bodies. They resemble ferments in the following particulars: (1) They are destroyed by heat. (2) They act in very dilute solution. (3) When repeatedly injected into animals in non-fatal doses they cause the body cells to elaborate antibodies which neutralize the toxin both in vivo and in vitro. (4) In the development of their effects a period of incubation is required. (5) It has been shown by Abderhalden, by optical methods, that they have a cleavage effect upon proteins. They split complex proteins into simpler bodies. In other words they have a proteolytic action. (6) They are specific in two senses. (a) They are specific according to the cell which produces them. Diphtheria toxin is elaborated by the diphtheria bacillus and by no other organism. The toxin of snake venom is a specific product of the poisonous gland of the snake, and this is further specific inasmuch as that produced by the glands of one species is different from that elaborated in another species. (b) They are specific in the antibody elaborated in the animal body after repeated injections of non-fatal doses. Diphtheria antitoxin protects only against diphtheria toxin, and not against that of the tetanus or dysentery bacillus, or that of snake venom.

The side-chain theory evolved by the genius of Ehrlich best explains the action of toxins and the production of antitoxins. Without subscribing to all the details of this theory, we believe that it is a biologic law that when a living cell is attacked by a destructive ferment or toxin it tends to elaborate an antiferment or antibody. This is one of the ways in which the living cell may protect itself. The formation of such antibodies in multicellular animals is one of the factors in the fine adjustment essential to harmony of action between different tissues and organs. It best explains the fact that the digestive organs do not harm themselves, and the antitryptic action of blood-serum is one of the most interesting and important phases of parenteral digestion.

The number of pathogenic bacteria which produce toxins, at least in appreciable quantity, is small, and the action of toxins and antitoxins in infections due to those organisms which do not produce such bodies is of minor importance. Since all bacteria, and in fact all living cells produce ferments, and since every ferment, so far as we know, may lead cells acted upon by them to produce antiferments, there

may be some toxin and antitoxin action in all infections, but in most bacterial infections such action is overshadowed by processes much more powerful in their effects.

In our opinion the action of the diphtheria bacillus may be stated as follows: The organism finds lodgement and the conditions for growth favorable in the upper air passages. Here it grows in mass and may kill by mechanical obstruction. It produces its soluble, diffusible toxin, which has the properties of a ferment and splits up the proteins of the body, setting free the protein poison. In case of recovery or in the production of antitoxin in animals, the body cells elaborate an antiferment or antitoxin which neutralizes the toxin and prevents its cleavage action. The bacilli in the throat are not destroyed by natural recovery or by cure with antitoxin, but the action of the toxin is prevented by the antibody. It is not, in our opinion, the toxin itself which kills, but a cleavage product which results from the action of the toxin on the proteins of the body.

All ferments are of cellular origin. This does not mean that ultramicroscopic forms of life or non-participate living organisms, if there be such, do not produce ferments. It would probably be better to say that all ferments are the products of living organisms and that there can be no living organism which does not produce its specific ferment. We cannot conceive of life without ferment action, because all living things must feed and food assimilation without ferment action is inconceivable. Food must be fitted for assimilation, and this is dependent upon ferment action.

Ferments are intra- and extracellular. All are formed within the cell, but some diffuse into the medium while others do not. In some instances at least cell permeation by the pabulum is essential to the feeding of the cell. In other instances it is highly probable that the ferment is accumulated on the cell surface and there acts upon the pabulum. In still other instances the ferment diffuses into the medium more or less widely from the cell which elaborates it. Many cells produce both intra- and extracellular ferments, and these are not necessarily the same. In some instances, probably in most cells, the intracellular ferment cannot be extracted from the cell or obtained in soluble form without destruction of the cell. This does not mean that it must exist in the soluble form before it can manifest its cleavage action. The pabulum may permeate the cell and in this location be split up by the intracellular ferment. We have insisted upon this as an explanation of the well-established fact that soluble proteins sensitize much more readily and completely than insoluble ones.

Before proceeding further it may be well to call special attention to some of the properties

of these ferments. The extracellular ferments are diffusible. They not only pass out of the cells in which they are prepared, but they diffuse more or less widely through the medium which surrounds the cell. This suggests that in molecular structure they are relatively simple. At least some of them may pass through membranes and collodion sacs, as is shown by the fact that bacteria and other proteins enclosed in such receptacles and left in a body cavity are destroyed. The extracellular ferments are, in part at least, filterable, passing with more or less readiness through porcelain. In their activities they are easily affected by modification in the medium through which they diffuse. The alexin of the blood serum is highly sensitive to the salt content of the serum, and by variations in this the activity of the ferment may be hastened, lowered, or wholly arrested. The same is true of bacterial ferments. In one species of animal a given bacterium multiplies with great rapidity; in another it grows slowly, while in a third it cannot grow at all. There are like variations in individuals of the same species. The extracellular ferments, at least some of them, are susceptible to slight changes in temperature. It is believed that every ferment has its optimum temperature, but the range in which continued activity is possible is narrow with some and relatively wide with others.

The intracellular ferments are non-diffusible, or at least less diffusible than the extracellular. They remain in the cells in which they are elaborated. They cannot be extracted from the cell by indifferent solvent. As a rule, they can be obtained from the cell only after partial or complete destruction of the cell. Some, probably most, are best extracted from the cell with dilute alkali, while others are best obtained by dilute acid. In either case the reagent must not be strong enough to destroy the ferment itself. They are non-filterable, or pass through filters slowly and imperfectly. We suspect that their molecular structure is relatively complex, or that they are more colloidal than the extracellular ferments. Under natural conditions the intracellular ferments act only on those bodies which are taken into the cell. The inclusion of bacteria by phagocytes is essential to the digestion of the former by the intracellular ferment of the latter. This is a phenomenon which may be seen, but cell permeation by foreign bodies is certainly necessary before such bodies can be acted upon by the intracellular ferments, and occurs with soluble proteins as well as with particulate ones. The intracellular ferment bears a wider variation in temperature, and is not so easily and delicately influenced by variations in the composition of the medium in which the cell exists. So far as we know the intracellular ferments do not

diffuse from living cells. They are, however, recognizable in the fluids of abscess cavities as the leukocytes disintegrate. We are of the opinion that they are essential constituents of the chemical structure of cells. The reason for this belief will be developed later. The extracellular ferments may be regarded as secretions of cells. Much has been written about cellular and humoral theories. In our opinion every living thing has a chemical structure, which we may designate as a cell if we wish, understanding that a cell is not necessarily something that can be seen, and that it may possess widely different degrees of liability, but we are quite certain that there is no ferment which is not the product of life processes. We have been somewhat surprised to find it stated that our own theory of protein sensitization or anaphylaxis is a humoralistic doctrine.

All ferments are products of life processes, and all life processes are more or less responsive to outside influences, to change in environment. In our opinion the most valuable fact that we have learned in the study of protein sensitization is that life processes manifested through ferment action are modified and may be modified at will by changes in environment. The blood-serum and organ extracts of normal guinea-pigs do not digest egg-white, but these fluids from an animal sensitized to this protein do have this action. The virus of smallpox is pathogenic to the man who has never had smallpox, and has not been vaccinated, but to the man who has had the disease or been properly vaccinated the virus of smallpox is non-pathogenic. We explain this, and in our opinion, the experiments of v. Pirquet have so demonstrated, that this is due to the fact that the ferments of the man's body cells have been so influenced by the disease or by vaccination that they have acquired a new function—that of digesting and thus destroying the virus of the disease. If this explanation be true, it opens up a wide field for the possible extension of the beneficial effects of preventive treatment.

There is another point of difference between intracellular and extracellular ferments, which is of the greatest importance in a study of the phenomena of infection. The extracellular ferments are comparable to those of the digestive juices of the alimentary tract in the higher animals. They roughly prepare foods for the cells. Their function is solely a lytic one. They break up complex proteins into simpler bodies, but the products thus formed are not, without further treatment, ready to be built into the structure of the cell. Proteins in the medium are rendered soluble by the extracellular ferments. They are so altered that they may be taken into the cell, but they are not so patterned that they are ready to be built into the struc-

ture. They are fitted for absorption, but are not ready for assimilation. The extracellular ferments are in a sense destructive agents. They break down complex molecules into simpler structures. The intracellular ferments are constructive. They are cell builders. They shape the material brought them and fit it into place. They build up specific proteins. They convert the raw material brought them into specific proteins, bacterial, vegetable, or animal. This does not mean that the intracellular ferments have no cleavage action. They chip the rough stone so that it fits in at the right place. It is by virtue of their activity or through their agency that cells grow and multiply. In case of an infectious disease the intracellular ferment of the infecting organism during the period of incubation converts man's proteins into bacterial proteins, and continues to do this with more or less success during the course of the disease. This seems to be accomplished in some diseases, at least, like typhoid fever, without any marked disruption of the cells of the man's body. The bacteria multiply rapidly during the period of incubation, and at this time the man is unconscious of the fact that his body is serving as a culture flask. We must conclude from this that the conversion of human proteins into typhoid proteins in the growth of the infecting agent is not accompanied by the liberation of the poisonous group in the protein molecule. This group, probably attached to other groups, or as a constituent of a more complex group, is used in the construction process. The poisonous group is common to all proteins. The synthesis of specific proteins from other specific proteins is accomplished without the liberation of the poisonous portion. It is one of the building stones, and changes in specificity do not occur in this, but in the secondary or characteristic group. This is, in our opinion, the explanation of the fact why incubation—a period of rapid reproduction in the infecting agent—proceeds without any recognizable disturbance in the health of the host. The typhoid bacillus, therefore, does not feed upon the cells of the man's body, but upon the formless, soluble proteins. Cell building is accompanied by the absorption of the poisonous group in the proteins serving as food. However, when the body cells become sensitized and elaborate a ferment which breaks down the bacterial cells, the poisonous group in the proteins of the latter is set free, and it is the effect of this poison that develops the symptom complex of the disease. The symptoms of one infectious disease differ from those of another largely according to the organ or tissues in which the infecting agent is located. In acute miliary tuberculosis and in typhoid fever, both conditions arising from a bacteremia caused by different organisms, the symptoms are only too frequently identical,

and it is only by bacteriologic methods, a suggestive history, or the findings of a pre-existing tuberculous focus in some part of the body that a differential diagnosis may be reached. A cholecystitis is the same, not only in symptomatology, but frequently in gross pathology as well, whether the infecting organism be the pneumococcus, the streptococcus, the colon, or the typhoid bacillus. The most skillful diagnostician cannot tell from the symptoms alone the specific bacterial cause of a meningitis.

During the period of incubation of an infectious disease, the infecting organism supplies the ferment, the body proteins constitute the substrate, the process is essentially constructive, no poison is set free, and there are no recognizable clinical symptoms. During the active progress of an infectious disease, the body cells supply the ferment, the infecting organism constitutes the substrate, the process is essentially destructive, the protein poison is set free, the symptoms of disease appear and life is placed in jeopardy.

Our work seems to show that the body cells, when overwhelmed with a foreign protein of the blandest kind—such as egg-white—may fail to function and death may result. There is no reason for suspecting that in these cases there is any cleavage of the foreign protein or the liberation of any poison. The body cells are simply clogged with the foreign protein and fail to function. We are not sure that this phenomenon has any parallel in the infectious diseases. There is, however, something closely related to it in cholera infantum, cholera nostras, and Asiatic cholera.

We have already referred to the fact that ferments may be modified in their activities. These modifications may be so radical that it is generally believed that cells may be trained, as it were, to develop new ferments. There can be no doubt that change in environment does alter activity as manifested through the ferments. As we have stated, it seems to be a biologic law that when a living cell is brought in contact with or permeated by a foreign protein, it tends to furnish a ferment which will digest and destroy the foreign body. The ferments of the cells of man's body may be modified or new ones developed by (a) disease, (b) vaccination, and (c) sensitization. Many of the infectious diseases give immunity to subsequent exposure. In some of the chronic infectious diseases the altered behaviour of the body cells to the infecting agent is evident even while the disease continues.

DISCUSSION.

DR. J. H. AGNEW: I have nothing to add that would be of any particular interest. I am always glad to hear Dr. Vaughan speak of this work, because I had the privilege of working with him, isolating some of the amino-acids of the cell substance of the colon

and tubercle organisms. It appears from Dr. Vaughan's remarks this evening that this feature, the structure of the protein of bacterial cellular substance, is of prime importance. It has been thought that bacterial proteins were simple substances but it has been shown in Dr. Vaughan's laboratory that they are quite as complex as proteins from other sources and therefore the same phenomena may be expected from them as from other proteins.

PROGRESSIVE BULBAR PALSY, ASTHENIC TYPE. (MYASTHENIA GRAVIS).

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A woman, age thirty-nine years, was admitted to the Hospital of the University of Michigan on February 5, 1914, complaining of marked difficulty in speech and deglutition. Her family history was negative; no member of her family, a large one, had any similar condition. She had an appendiceal abscess when twenty-five years old and was operated upon. The following winter she had "peritonitis." Menstruation began at fourteen, was regular but painful, sometimes accompanied by syncopal attacks. She was married at thirty and five years later gave birth to a dead fetus. Following her pregnancy the menstrual periods were less painful. While still in childbed she began having attacks of epigastric pain, nausea and vomiting, diagnosed later as due to "achylia gastrica and cholecystitis." She suffered from attacks of this sort until March, 1912, when she had the last one. Her present trouble began about one week after the last attack of the vomiting, when she noticed at dinner a difficulty in swallowing and a husky voice. Since then the condition has grown progressively worse except for an interval of a week about Christmas, 1913, when there was a slight remission. She had been in bed for ten weeks on account of her general weakness and has had to be tube fed for about the same length of time. There has been no pain in any part of the body at any time during this illness and no headache.

Examination made after her admission to the Hospital gave the following results. The patient was lying in bed with a general appearance of great exhaustion. She was markedly emaciated. Her face was expressionless. Her eyelids drooped about half way over the pupils. This drooping is said to be variable, much worse some days than others. There was no palsy of the extraocular muscles and the pupils reacted to light and in accommodation. There was slight nystagmus. There was no apparent weakness in the masseter or temporal muscles and sensation to touch and pinpoint on the face was normal. She could

not wrinkle the forehead but could corrugate the eyebrows slightly. The eyelids could not be closed completely and could not be held closed. She could draw back both corners of the mouth slightly but she could not whistle nor spit. She said that she felt a drooping of the lower lip and saliva occasionally drooled from the mouth. There was no impairment of hearing but bone conduction was lowered on both sides. The pharyngeal wall was anesthetic and the soft palate did not rise in phonation. There was no paralysis of the vocal cords (Dr. R. B. Canfield). The tongue could only be protruded slightly beyond the teeth and had a peculiar appearance in that the tip of the tongue was narrow and this narrowing extended about an inch to an apparent constriction about the tongue. There was no longitudinal growing as ordinarily seen in lingual atrophy and when the tongue was grasped with the fingers and pulled forward the constriction disappeared. There was no paralysis of the neck nor extremities and no sensory disturbances but the patient was so weak that she could not sit up nor hold up her head without support. There was no incontinence of urine or feces. There was marked general emaciation. The tendon reflexes were normal in the upper and lower extremities and there was no Babinski reflex. Mentally, she was perfectly clear and showed no retardation of thought. Articulation was much impaired; speech was slurring, typically bulbar and almost unintelligible. She had to be tube fed. The electric reactions in the facial muscles and in the tongue were normal both to the faradic and galvanic current. After tetanising the tongue about one minute with the rapidly interrupted faradic current, the irritability diminished but was rapidly recovered by a few seconds rest, (myasthenic reaction). Repeated contractions by the kathode of the galvanic current (100 contractions at one second intervals) caused no change in the amount or character of the contraction in the muscles of the face or tongue. Her heart and lungs were apparently normal. She frequently had epigastric distress after being fed and sometimes vomited. Her bowels were constipated. The temperature was normal. Pulse rate varied from 90 to 160. The changes in the pulse rate were sudden and not explained by any change in temperature. The attacks of tachycardia would last from twelve to twenty-four hours and were accompanied by the increased respiratory rate. Respiration was from 20 to 40 per minute. The urine showed no albumin nor casts and no sugar. The blood count gave 3,950,000 red blood cells, 12,950 white blood cells, and hemoglobin, 78 per cent. Miescher method. Differential leucocytes count: neutrophilic polynuclears, 81%; eosinophiles, 1%; degenerates, 6%; transitionals, 5%; large lymphocytes, 7%; small lympho-

cytes, 6% (patient menstruating). The Wassermann reaction on the blood was negative. The lumbar puncture showed the spinal fluid to be clear and colorless. The pressure was about normal. Only one lymphocyte was found in 5 cmm. The Nonne-Apelt reaction phase I, was negative; phase II, negative. The reducing substance was present in about normal amount. The Wassermann reaction on the spinal fluid was negative. The gynecologic examination (Dr. Reuben Peterson) showed retroversion of the uterus and pelvic adhesions. The ophthalmologic report (Dr. Walter R. Parker) was—"Retained nerve fibers, more marked in the left than in the right eye. Slight arteriovenous compression."

It is necessary to take into consideration a number of conditions in diagnosing a case like this but most of them are excluded easily. Post-diphtheritic palsy and pseudo bulbar palsy, due to bilateral cerebral lesions, are readily excluded by the history, and the same is true of so-called apoplectic bulbar palsy. The facio-scapulo-humeral type of muscular dystrophy gives a somewhat similar appearance to the face but does not cause difficulty in swallowing. Syringobulbia and brain tumor pressing on the medulla might give rise to the bulbar symptoms but the other signs of these affections are absent. Syphilitic disease of the brain might be thought of because of the history of a still birth and the reduction in bone conduction. However, there were no other signs of syphilis.

There are two types of bulbar palsy that are progressive. In the first of these atrophic changes are pronounced, the affected muscles show the electrical reactions of degeneration and the ocular muscles are not involved. This type occurs late in life, as a rule in the fifth and sixth decennium. A second type is the asthenic and myasthenic type. It occurs in younger individuals; there is usually ptosis, no marked atrophy and the electrical reactions are not those of degeneration but are the so-called myasthenic type. In the first type distinct pathologic changes are found in the medullary nuclei; in the myasthenic type such changes are not usually found. Dr. Kuh has recorded a typical case of this kind in which thromboses were present in the medulla. The prognosis is unfavorable in both types. Oppenheim records a fatal termination in twenty-six out of twenty-eight cases of the myasthenic type but it is quite possible for pronounced remissions to occur.

The etiology of this condition is not determined. It would seem as though congenital tendencies might play a part. In many of the reported cases anatomic peculiarities are noted—extra fingers or toes, web fingers, et cetera. In this case the retained nerve fibers is a peculiarity of the same order. Persistent thymus

and thymus tumors are frequently found at autopsy in these cases. Autotoxemias, chronic infections and tumor toxins have been regarded as etiologic factors.

REPORT OF A CASE OF RELAPSING FEVER.

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History.—The patient, Dr. C. P. age 37, was admitted to the University Hospital, January 19, 1914, complaining of headache, severe backache and a feeling of malaise. The paternal grandfather died of tuberculosis and twenty-five years ago his father died of pulmonary tuberculosis at the age of 48. The patient has had the usual children's diseases. For the past two years he has lived in Augusta, Georgia. He has never had malaria.

Present Illness.—The present illness began January 15, 1914 with malaise but he was not sick enough to stop work. Two days later he complained of "feeling miserable" and of headache over the eyes; also at this time he had an aching pain in the lumbar region. January 18, patient became much worse, taking to his bed with a poor appetite, complaining of feeling dizzy when on his feet. His temperature at this time was 101°. He had no shaking chills, sore throat, coryza, sweats nor vomiting; the bowels were regular and there was no urinary trouble.

Examination.—On examination the temperature was 102.4°, pulse 104, respirations 22. The patient was underweight and poorly nourished, somewhat anemic. There was no general glandular enlargement. Examination of the chest disclosed slight impairment to percussion over the right apex with harsh vesicular breathing and definite crackling râles, which were persistent after coughing. The heart was negative. A few crackling râles were heard over the right apex behind. The spleen was not palpable and the liver was apparently not enlarged. The urine and the stools were negative.

Course.—The temperature dropped to normal on the evening of the day of entrance and remained normal until discharge. This occurred by crisis, dropping from 101° to 98.6° in four hours. An examination of the blood showed 4,600,000 red cells, 3,000 white cells and 85% hemoglobin. Differential count; polymorphonuclear cells 62%, large lymphocytes 30%, small lymphocytes 6%, transitionals 2%; one normoblast and 8% degenerated large lymphocytes were seen. While making the differential count and looking for malarial parasites, one characteristic spirillum was found.

Diagnosis.—A diagnosis of relapsing fever was made and the patient given three tenths of a gram of neosalvarsan that afternoon.

Relapse.—The patient remained well up to February 1st., when he began to have a feeling of malaise and headache. He kept about until February 8th., when his headache became so severe as to make him take to his bed. He noticed pain in the lumbar region and considerable soreness in different parts of the body, including his testes. There was no definite chill. His temperature taken February 4th., was 99°. On February 5th. he had a temperature of 100° and on the 6th a temperature of 101°. From the 4th of February he ran a continuous, irregular temperature and on Monday, February 9th, he entered the Dermatologic clinic for another treatment. His temperature fell by crisis that same night. The spirillum was looked for in the beginning of his last illness on numerous occasions by Dr. Novy and his assistants. He was so sick on February 8th, that examinations on this day were omitted. A smear was taken on February 9th., but no spirillia were seen. I am sorry that the patient did not notify me of this recurrence, as he promised to do before he left the Hospital.

It is well known that the relapsing fever of America shows very few organisms in the circulating blood. I wish I had had an opportunity of searching for the organisms by centrifuging ten cubic centimeters of this patient's blood after laking the red blood cells. This method has worked very well in isolating tubercle bacilli and the embryos of trichinae.

The patient had been working in the bacteriological laboratory of the University of Michigan, although not directly with the spirillum of relapsing fever, but claims to have been bitten by rats inoculated with this organism. There is some evidence to show that the disease can be conveyed by contagion, such as clothing or the handling of the bodies of patients who have died of the disease. It has been definitely proven that the disease is transmitted by ticks, head lice, and possibly the bed bug. In 1905, Carlisle of the Bellevue Hospital reported two cases of relapsing fever, the second the result of the bite of an infected monkey inoculated with the organisms from the first case. S. T. Darling in the *Archives of Internal Medicine*, 1909, reports five cases of relapsing fever inoculations occurring either through the skin or due to the bites from infected monkeys.

Relapsing fever is a specific infectious disease frequently occurring in epidemics. An attack is characterized by a fever of about six days duration, followed by a remission of the same period, then another attack of fever, occasionally a third attack, rarely a fourth or fifth. The disease is self limited, rarely fatal in itself, death usually being due to complications, of

which pneumonia is the most frequent. The small mortality is found in the debilitated and aged. The incubation period is very variable, usually from five to fourteen days. There are very few prodromal symptoms, generally a feeling of malaise, the disease setting in abruptly, usually with a chill, followed by a rapid rise of temperature, rapid pulse, accompanied by continued and severe headache, dizziness and pain in the back. The general condition grows rapidly worse, forcing the patient to bed on about the second day. The appetite is lost, other gastric symptoms varying considerably. The headache continues with marked insomnia. There is usually enlargement of the spleen and liver and frequently a polymorphonuclear leucocytosis. Often on the sixth day there is a sudden fall of fever, by crisis, which usually occurs at night. About thirty or forty per cent. of the patients have only one attack, but during a relapse the organisms may again be isolated from the blood. Not infrequently the second attack is worse than the first.

The specific cause of the disease is due to an organism described by Obermeier of Berlin in the year 1873. The parasite is a delicate, colorless, spirally-twisted organism, resembling a fine thread of fibrin, about ten to fifteen microns in length. When found in the blood it is easily seen moving about among the red blood corpuscles, apparently never quiet, progressing forward or backward. No definite structure has been made out, although in some instances, a granular or beaded appearance has been noted. This was observed in our organism which was treated with Hasting's stain. The number of organisms found from day to day varies greatly. As a rule there are few early in the attack, but they gradually increase in number, reaching the maximum shortly before the crisis, when they decrease rapidly and may completely disappear. The cause of the disappearance of the organisms is unknown. The disease can be conveyed to another individual by inoculation of the blood during a paroxysm. Certain insects, such as bed-bugs, may suck the spirochete and in this way produce the disease by biting. Dr. Novy has suggested that there are probably four forms of relapsing fever in man. There are no characteristic pathologic findings in patients dead of the disease.

Intravenous injections of salvarsan or neosalvarsan in moderate doses, usually abort the disease or prevent further attacks.

DISCUSSION.

DR. FREDERICK G. NOVY: I am very glad to discuss this unusual case. The question of how these infections occur in the laboratories is an interesting one. The transmission by insects, the natural mode of infection, is practically excluded in these laboratory accidents, unless the work actually involves the study of such parasites. In some instances there

is no evidence at all of a bite caused by an experimental animal, such as the monkey or rat. There may even be no evidence of an injury, such as a scratch or cut which would facilitate the entrance of the specific organism. Under these circumstances one is obliged to seek for an explanation of such infection in the known fact that spirilla can penetrate through the unbroken mucous membrane and even through the unbroken skin. A minute drop of infected blood brought into contact, in some way, with the mucous membrane of the mouth or nose, or with the conjunctiva, is sufficient to bring about an infection. As a matter of fact this is one stage in the natural mode or transmission of the disease.

As regards the natural mode of transmission, I would like to emphasize one point already mentioned, and that is that certain insects are the natural means for the spread of the disease. We have two good illustrations of this fact. The tick fever of equatorial Africa is produced entirely by the bite of a tick, the *Ornithodoros moubata*. In Northern Africa and in Europe this tick does not exist and hence some other intermediate host must be sought for. The work carried on in Eastern Europe has not helped materially to clear up this point. In Northern Africa, more especially Tunis, the local relapsing fever has been shown conclusively to be spread through the agency of the body louse. Nicolle and his co-workers, in Tunis, demonstrated first that the mere lines of lice which had fed on infected animals did not produce the disease in man or monkeys. In other words, the bite itself was inoffensive although there was every reason to believe that the louse was the means of transmission. They found that the spirilla which were sucked up with the blood by the louse, soon disappear from the intestine and cannot be detected anywhere for a period of 8 to 19 days. The spirilla then appear, not in the gut, but in the lacunar cavity. Since infection of man does not follow the mere bite of such infected insects; nor result from fecal deposition on or about the wound, in the process of feeding by the insect, it became apparent that infection could only occur through the crushing of the biting insect and the consequent liberation of the spirilla. These may then come into contact with the wound; they may be carried by the finger tips to the eye, mouth, or nose, and thus give rise to the disease. These facts have been ascertained by direct experiments upon the laboratory staff.

A point that I want also to call attention to is the extremely beneficial results obtained with salvarsan. If there is any thing in which salvarsan is good, it is in relapsing fever. In this particular case there was a relapse, following the first injection. An attack of the disease, or a relapse, can be jugulated by an injection of salvarsan, if given at the onset of the symptoms.

A CASE OF KORSSAKOW'S PSYCHOSIS COMPLICATED BY CEREBRO- SPINAL SYPHILIS.

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Mr. M. was found on Sunday morning December 9, 1913, in an unconscious condition in the back room of a downtown saloon. At first his friends thought that he was drunk as usual but this idea was abandoned when his condition

did not improve. During the afternoon he had a series of convulsions and his people became alarmed. Being unable to arouse him out of his stupor, it was finally deemed advisable to send him to the University Hospital. He was admitted to the Medical clinic at nine in the evening. At that time he had a rectal temperature of 104°; he was stuporous and unresponsive. Shortly after admission he vomited. The vomitus was non-specific; however, to make sure, his stomach was thoroughly washed.

The history of the case was meager and one could, therefore, only speculate as to the probable trouble. Was he poisoned as his parents suspected? Did he have uremia, diabetic coma, apoplexy, epileptic stupor, cerebral syphilis or beginning delirium tremens? Any of these conditions might well produce a stupor with convulsive seizures. Inasmuch as there was no difference in the muscular tonus of the two sides, no stertorous breathing, and the temperature was not normal or subnormal, apoplexy was practically ruled out. During the following morning, he had a series of six convulsions which were epileptiform in type. His temperature was 103.6°, his breathing rapid. On the whole he was quiet. He did not speak, but when touched, he would look around. The examination of the heart, lungs and abdomen was negative. His urine contained a heavy trace of albumin and numerous casts, but no sugar, diacetic acid or acetone. Since he really was not comatose, and showed no evidence of air hunger, diabetic coma was improbable. The absence of diacetic acid and acetone in the urine ruled out that condition definitely. Uremia was not so easily disposed of; for that disease may commence suddenly, often with a loss of consciousness and epileptiform attacks. Usually the patients are confused, unclear and delirious, though sometimes they may be sullen and apathetic. But since the urine showed only a trace of albumin and was not loaded with casts, it was not thought necessary to make a urea determination of the blood.

The microscopic examination of the blood added still another possible diagnosis. The examination made by Dr. H. Schmidt showed 3,400,000 reds, 24,000 whites, mostly polymorphonuclear and a hemoglobin of 83% Miescher. The study of stained blood smears revealed marked aniso-cytosis, considerable polychromasia and large numbers of basophilic stipple cells. No nucleated reds were seen. In other words the blood picture strikingly resembled that of lead poisoning. This was, indeed, interesting, for plumbism might well produce the entire symptom complex. The mental and cerebral symptoms in lead poisoning, classed under the head of encephalopathia saturnina, are usually hemianopsia, delirium, coma and convulsions, mostly of the type of general-

ized epilepsy. Though he had occasionally assisted in the painting of barns, it was learned that he had not done any work of that kind since June. Examination showed neither anemia, wrist drop nor a lead line on the gums. Subsequent chemical analysis did not reveal even a trace of lead in the urine and so the hope of a striking diagnosis vanished.

During the afternoon he became so restless and apprehensive that it was difficult to restrain him in bed. Fearing delirium tremens, he was committed to the Psychopathic Hospital on an emergency order. Soon after his transference, he became quieter and took liquid nourishment in large quantities. With the aid of a dram of paraldehyde, he slept six hours the first night. On the following morning his bowels were exceedingly loose. He co-operated to some extent with the attendant. He looked apathetic and sleepy. To most questions, he answered with absolute indifference "Oh, I don't know." Two days later his temperature again went up to 103°, the breath sounds over the right side of the chest were harsh and the expansion somewhat decreased. A central pneumonia was suspected; however, the temperature did not stay up long and the breathing soon became easier. During the next three days, he improved considerably. He looked and felt better and answered questions more promptly. He thought it was Thursday, August, 1999, and that he was over Myer's saloon in Ann Arbor. He asked for Miss S. and said that he had seen her several times that morning. He gave Washington as the president of the United States and said that he had been elected by the progressives. When questioned later regarding his drinking habits, he admitted that he had indulged heavily for the last ten years. Usually he consumed from five to six bottles of beer a day. About once a month, he went on a drunk for two or three days. On these occasions he mixed his drinks. This last time he got in with some cronies from Jackson and they were together Thursday and Friday, consuming half a barrel of beer and several quarts of whiskey. He remembered being at Myer's beer-house after they had left, but for the time that elapsed between Friday and Thursday morning he is amnesic.

Judging from the account obtained from his mother, it is evident that he comes from a family of low type with a history of alcoholism and pauperism. The maternal grandfather was a heavy whiskey drinker and an occupant of the Washtenaw county house for years. Two brothers of the mother, the maternal cousins and one of the patient's brothers are heavy drinkers. The patient is said to have developed normally. It is not known how much schooling he had. He stopped somewhere around twelve because of his unwillingness to continue. He

worked as a farmhand and later as a common laborer. He commenced drinking at about nineteen, but it was only during the last five years that he has drunk to excess. He takes something every day and according to the mother he is intoxicated four or five times a week. Without liquor he is extremely nervous and practically helpless. During the last year, he has done odd jobs, helping around saloons, painting a barn occasionally and collecting junk. There is no history of epilepsy in his own past life. Epileptic stupor was, therefore, unlikely and in view of the subsequent developments, entirely out of the question.

He is a man thirty-nine years of age. Examination revealed an enlarged liver, but normal blood pressure and normal vessels. There is a smooth scar back of the corona, which he said resulted from a hard sore four years ago. The left pupil is a little larger than the right. Both react fairly well to direct and consensual light stimuli and in accommodation. The extraocular movements are fairly well performed. The acuteness of his taste is diminished. He shows considerable hyperalgesia and hyperesthesia. He is sensitive over the nerve trunks of the extremities. The left knee jerk is present and about normal. The right knee jerk and the left Achilles jerks were absent even on re-enforcement. There was a questionable Babinski on the right. There were, therefore, numerous polyneuritic disturbances which might well be produced by chronic alcoholism. But why did he not clear up after his acute delirious episode? Was he passing into Korsakow's psychosis? This condition might well be expected in view of his heavy drinking. Twenty-five per cent. of the cases of Korsakow's psychosis according to Kraepelin do begin with an acute delirium, sometimes with epileptiform attacks. Instead of clearing up within a few days, they pass over into a chronic state showing apathy, irritability, marked memory defect, confabulation and polyneuritic disturbances.

Re-examination of the urine December 11, 1913 showed a trace of albumin and numerous granular casts. The blood count made on the same day showed 4,200,000 reds and 24,000 whites. Five days later the white cell count had fallen to 20,000. On neither occasion could any stipple cells be found in the smears. The cerebrospinal fluid examined on December 16 contained 38 cells per cmm.; the globulin test was positive in a dilution of 1 to 10; Nissl-Esbach 3.0. The Wassermann was four plus positive both on the blood and the spinal fluid. Here was another complicating factor. Was his attack due to a combination of alcoholism with general paralysis? Was that the reason he did not clear up from his acute delirium? But his infection was only four years ago and the

peculiar polyneuritic disturbances could hardly be produced by general paralysis.

For two weeks after admission to the Psychopathic Hospital he continued to be disoriented, always thinking he was over a saloon and that he had been there about four days. He was unable to return numbers of five digits and when short stories were read to him, he could not repeat them. He was unable to detect the most evident absurdities. He had some difficulty with the usual test phrases. Even in writing his name he made numerous mistakes, such as reduplications and transpositions. He also showed a slight tremor. He could not write Ann Arbor or the word saloon. In writing the abcs he only got as far as b and ended with *or*, still thinking that the physician wanted him to write Ann Arbor.

On December 20th, early in the morning, he had five severe epileptiform convulsions, each lasting about four minutes. He was unconscious for over two hours, but after that he was as clear as usual. By the third of January, 1914, he had gained five pounds in weight and as a consequence he had improved considerably in appearance. Though oriented, he still was unable to repeat short stories when they were read to him, but when a story was told him in simple slang fashion, he gave most of the details fairly accurately. There was no tendency to confabulation. He did very poorly in writing the alphabet. He rarely got beyond d or f and then often repeated many of the letters given previously. He excused himself by saying he never went to school more than three terms. In writing his name, he still showed a slight tremor and added an extra letter. Re-examination January 10th showed that the reflexes which had been absent had returned, though they were still much diminished in comparison with their fellows. His station and gait were normal and there was not even a questionable Babinski. Though he could add and subtract successive sevens correctly, he could not figure out what year it was seven years ago. A second lumbar puncture made January 3rd showed 32 cells per cmm., globulin positive in dilution of 1-5, Nissl-Esbach 1.5 and again a four plus positive Wassermann. Both the cell count and the globulin were, therefore, less than on the first examination.

During the last month he has continued dull and uninterested. Whenever he cannot answer questions, he becomes irritable and refuses to co-operate further. He knows the name of only one of the physicians. Even when speaking of his friends downtown, he rarely is able to give their names. He is correctly oriented and knows approximately how long he has been at the Hospital. He has no conception of the seriousness of his condition before coming to

the Hospital; he knows no more about it than what his father told him. His perception is better on the whole and he can figure out what year it was seven or thirteen years ago. There is now no noticeable articulatory defect in his spontaneous speech. The urine and blood are negative. A third lumbar puncture made on February 7th showed a cell count of seven, Nissl-Esbach 1.2 and globulin positive in equal quantities but negative in dilution of 1 to 5. The Wassermann is still four plus on the blood and the spinal fluid. The cell count, globulin, and Nissl-Esbach have, therefore, come down to practically normal. These findings make the presence of general paralysis very improbable.

According to the reports of Assmann (2), Nonne and Holzmann (3), Betz (4) and Peyton Rous (5), the cell count, the globulin and albumin are normal in cases of chronic alcoholism and Korssakow's psychosis. This agrees with the fluid findings of the four cases of chronic alcoholism (two of which were cases of Korssakow's) that were punctured at the Psychopathic Hospital. In two cases the Nissl-Esbach was slightly increased. But inasmuch as this patient has a persistent Wassermann on the spinal fluid, cerebrospinal syphilis cannot be excluded. Since there was a progressive improvement in the cytologic and chemical findings of the cerebrospinal fluid, one might infer that a latent luetic process had become temporarily active by reason of the alcoholism.

We have then a man who has been a heavy drinker for years, taken down suddenly with epileptiform convulsions, passing over into a stuporous state and then into an atypical delirium. This gradually cleared up, leaving him dull, apathetic, and with polyneuritic disturbances, marked defect in his memory and discrimination, but showing no tendency to confabulation.

In view of these findings, the diagnosis of Korssakow's psychosis combined with cerebrospinal syphilis seems warranted.

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2. Assmann, *Deutsch. Ztschr. f. Nerventh.* XL. 131.
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4. Beltz. *Deutsch. Btschr. f. Nerventh.* XLIII. 76
5. Peyton Rous, *Am. Jour. Med. Sc.* CXXXIII. 571.

DISCUSSION.

DR. H. B. SCHMIDT: This patient entered the Medical clinic as an emergency case. An examination of the blood disclosed a considerable amount of stippling of the red blood corpuscles. As there was practically no anemia, lead poisoning was considered as a probable cause of his coma and convulsions. There was no lead line present, but as we know that in either acute or chronic intoxication from lead, especially in alcoholics, delirium, delusions

and coma may be present, we still considered lead encephalopathy as a diagnosis. A sample of his urine was examined by Dr. Vaughan on two occasions and found negative for lead.

He remained in the Medical clinic only a short time, about thirty-six hours, and re-examination of the blood with Unna's stain showed that the stippling had almost completely disappeared and was not typical of lead poisoning, in that the granules did not take the red stain. This is very important in differentiating the stippling of the red cells seen occasionally in a normal blood from that seen in severe anemias and lead poisoning.

AN ESTIMATE OF THE VALUE OF THE WASSERMANN REACTION TO THE GENERAL PRACTITIONER.

UDO J. WILE, A.B., M.D.,

Professor of Dermatology and Syphilology. University of Michigan.

The last decade in medicine has seen an enormous growth in knowledge concerning syphilis. Indeed, it may be said that in no other field of medicine, either clinical or experimental, has there been greater progress made than in the study of syphilis. The discovery in 1905 by Schaudinn and Hauffman, of the infecting organism, and of the complement fixation test of Wassermann were forerunners of an epoch of research which has resulted in a great accession of knowledge to the practitioner of medicine and incalculable benefit to mankind.

It was my good fortune to have been one of the first American students of the complement fixation test, to have performed this work under one of Germany's foremost serologists. It has fallen to my lot of late on several occasions to defend this wonderful laboratory test before early sceptical audiences. I have recently expressed myself as favoring, for the protection of the hospital staff, a routine, compelling all entrants into hospitals to submit to the Wassermann test before their admission. I mention this positive stand which I have taken to offset any idea which may arise from the theme of my paper this evening. I wish to point out herein that notwithstanding the enormous gain which the complement fixation test has brought to clinical and experimental medicine, its wide and indiscriminate use has not been entirely without disadvantage to the practicing physician.

A proper estimate of the value of the Wassermann reaction to the practicing physician must take into account, first, the limitations of the reaction itself, and, second, its judicious application. With regard to the first factor, it must be admitted at the outset that there is a great variability in the technic of the reaction as it is carried out. There is even a daily difference in the efficiency of the various reagents. Secondly, in a reaction so complicated and so delicate, there are constant sources of error

cropping out, and lastly, the question of the personal equation enters into the interpretation of the test. For example, in a doubtful case, what to one observer's eye and judgment is read as a partial hemolysis, may be interpreted as doubtful by him; a second observer might read the same test as faintly positive and a third might regard it as negative. It has been my custom in important cases to divide the specimens and to compare the readings of two different observers of the clinical findings and thus place a check, as it were, on the result of the test.

First and of paramount importance, the practicing physician who wishes to employ the Wassermann reaction must know the ability of the laboratory technician who is to carry out the test. Within the past few years, numberless advertising laboratories and even druggists have placed their resources at the command of the practitioner for the performance of the complement fixation test. I am satisfied that for the most part their work is entirely unreliable.

A second point of no less importance has to do with the limitations of the test itself. Far too often is the fact forgotten that in the first stages of the disease, and practically during the entire period of the development of the chancre, the test is uniformly negative. A test taken at this time is, therefore, useless. It is regrettable that a negative outcome at this period is still interpreted as negating syphilis, to the chagrin of the physician at a later date, and occasionally to the irreparable damage of his patient.

During the secondary period, the reaction may be said to be more uniformly positive, and probably the fewest errors are made during this period. But even here, a negative outcome may trap the unwary. The most malignant, precocious types of syphilis are occasionally characterized by a negative reaction. During the past year I have seen two such cases—in the first a profuse follicular, and in the second a rupial, syphilid. Both were frankly negative in the blood. In the tertiary stage of syphilis, according to different observers, from fifteen to thirty per cent. of all cases react negatively. Taking the lowest estimate, the physician who places his sole reliance on the outcome of the test, takes a fifteen per cent. chance of being wrong. In hereditary syphilis with manifold lesions, practically all cases react positively, but in the latent stage, a negative reaction is not infrequent, and it often occurs that children whose blood at birth is negative, develop syphilis within a few weeks after the test has been taken.

Of great value to the general practitioner is the employment of the test upon wet nurses. It goes without saying that no woman should

be engaged for a healthy infant who has not first submitted to the Wassermann test.

A not uncommon error where entire reliance is placed upon the outcome of the test is found in the fact that the patient may have a latent syphilitic infection which is in no way connected with the condition for which he requires active treatment. In particular does the diagnosis of abdominal and thoracic neoplasms thus suffer from a lack of clinical study. The presence of a positive reaction in such cases is, it is true, evidence of a syphilitic infection, but only presumptive evidence that the condition in question is due to syphilis. In cases such as this, in fact in all obscure cases, the result of the test should be carefully weighed against the clinical features of the disease.

The greatest importance, however, attaches to the value of the test as a guide to the efficiency of treatment. A decade ago and before, careful medical men followed the teaching of a great syphilologist who taught that syphilis must be treated at least two years, and better, three. This was a purely arbitrary rule based upon a vast experience which showed that if treatment were carried out energetically for this period of time, patients remained well, had no late lesions, and could safely marry and be the progenitors of healthy offspring.

We now know that some syphilitics get well within a year; that others require two or three or more years to cure; and that some, indeed, never get well. It was an early observation in the history of the complement fixation test that a positive reaction tended to become negative under treatment, if the latter were efficient and persisted in. Frequent reactions, therefore, taken during the periods of repose in treatment serve as an excellent guide as pointing to the efficiency of our treatment. Here again, however, a word of caution. A negative test taken during the time that the patient is under treatment is of no significance, and no test should be made until at least from four to six weeks following cessation of all treatment. During the past week, I was consulted by a man who came to me, as he said, for a blood test. He had contracted syphilis last July. A blood test taken one week after an intravenous injection of salvarsan, and at a time when he was taking mercury, was said to be negative, and his physician pronounced him cured. There was no need for a second blood test. The examination revealed recurrent lesions in the mouth and a papular syphilid of the chin.

In general, it may be said that a negative reaction gains in value and significance with each succeeding negative test, and a cure should never be pronounced until the reaction has remained negative on several successive trials.

While it is undeniably a fact that a persistent positive Wassermann means a latent infection,

it is nevertheless also a fact that occasionally patients in a latent stage of syphilis will have a positive Wassermann reaction which remains so notwithstanding all forms of treatment. Such cases not infrequently remain in perfect health. They marry with impunity and become parents of healthy children. Such cases occur particularly in those in whom treatment is begun late in the course of the disease. While it is a fact that a positive Wassermann in the active and early stages of the disease means the occurrence in the blood of antibodies or immune substances which are called forth by the presence of the infection itself, yet it appears not unlikely that in these cases with persistent Wassermann reactions which resist all forms of energetic treatment and yet remain perfectly well, the presence of complement binding substances is due to a chronic change in the blood not necessarily activated by living spirochaete. Personally, I have seen a number of such cases in which matrimony or the resumption of marital relations has resulted in perfect children and in nontransmission of the infection to the mate.

There is, as you all know, in a neighboring state, a law which requires all candidates for matrimony to submit to a Wassermann test. Although the wisdom of such a law is unquestionable, its application at the present time is difficult. While a step in the right direction, it is, if carried out on the blood alone, really a half-way measure. To give a man or woman a clean bill of health, not only should a test be made on the blood but also upon the spinal fluid. A certain percentage of cases of cerebrospinal syphilis, active and latent, is negative in the blood and positive in the spinal fluid. Obviously, permission to marry should be withheld in such cases as these. Moreover, the ends of such a law may be defeated by the fact that the reaction may be temporarily inhibited by active treatment coincident with the time of the taking of the test. A careful physical examination at the same time will usually, offset this possible error. It is, perhaps, a matter of a short time when all states will have similar statutes on their books, and for uniformity of results, it will then be necessary to establish state laboratories of serology.

I wish now to turn to the second axiom of my theme—the judicious application of the test. While it is true that the Wassermann test has cleared up many hitherto obscure conditions and placed them on a syphilitic basis, it is nevertheless also true that syphilis in all its forms was recognized before the days of laboratory aids. The statement that the indiscriminate use of this test in practice is making for poor clinicians, is not, I think, too broad. We are losing in medicine that fine type of mind which made for keen observation and deductive reasoning.

There is no cutaneous nor mucous membrane syphilid which requires a Wassermann test for its diagnosis. The careful surgeon can and should be able to differentiate gumma from sarcoma or tuberculosis of bone. A discriminating internist of the older school required no Wassermann test to diagnose syphilitic cirrhosis or early syphilitic anemia. The countless manifestations of syphilis are not difficult of clinical recognition if care be given to their study.

The teaching of syphilis in our schools should be, I believe, toward the development of that faculty of keen observation and deductive analysis which characterized the clinician of an older day. If more time were expended in developing such faculties, we would then be equipping students who were capable of recognizing a chancre without a dark-field, and who would reflect twice before operating on gummatous lesions.

In conclusion, permit me to advise the general practitioner to make use of the Wassermann test, but to use it very judiciously; to be sure when using it of the laboratory technician's ability; to avoid its frequent use as a diagnostic aid by acquiring through study of syphilitic lesions and manifestations the diagnostic touch and eye which makes the unravelling of disease processes ever a new and fascinating study.

DISCUSSION.

DR. WILLIAM A. PUSEY, Chicago: I am glad to hear Dr. Wile discuss the Wassermann reaction and I am surely in accord with most of what he says. There is one point that Dr. Wile made which should be especially emphasized—that the Wassermann is not always positive in the presence of active syphilis. Some syphilographers insist that they get a positive Wassermann in all active syphilis. If there is a chance of twenty per cent, negative reactions in the presence of active syphilis, one is up against the possibility of making a great many mistakes. I am reminded of a case I saw a year ago—a man with a perfectly clear ulcerating syphilid of the leg. He had a negative Wassermann and, because of this,

his doctor excluded syphilis. I said to the man, "This is syphilis." "It is not syphilis," he said. "I wish it *were* syphilis—I might get well if it were I had a negative Wassermann. I haven't had syphilis for twenty years."

I do not agree with Dr. Wile in his statement that repeated negative Wassermanns indicate that the patient is well of syphilis. In McIntosh and Power's book there is a discussion as to when a patient can be pronounced cured of syphilis. "Only after repeated negative Wassermanns extending from one to two years, and often conscientious syphilologists can only say so after twenty years." I should say that conscientious syphilologists could *never* be sure that a patient is absolutely well of syphilis. Regardless of the disappearance of symptoms, the syphilitic infection may remain and reappear years later.

Dr. Wile says that no patient with a positive Wassermann is entitled to marry. As a matter of fact, for many years I have assumed that after five years of cessation of symptoms of syphilis, syphilitics could marry. Jonathan Hutchinson used to let most of his syphilitics marry after two years. Fournier allowed his to marry after five years. It is a rule, however, that may be followed by disastrous results. This means that a vast number of men marry after five years who have a positive Wassermann, for a vast number of syphilitics remain positive intermittently for life. Some of these patients marry and raise healthy families. In the face of that fact, however, I think that a man is not entitled to marry after five years with a positive Wassermann. We cannot give anybody absolute assurance of having healthy children, no matter who he is. In the present condition of our knowledge, I think we are not warranted in taking that hard and fast stand with regard to the Wassermann.

DR. WILE (closing the discussion): Dr. Pusey and I do not differ very much after all with regard to the ability of patients with a permanent positive Wassermann to marry and have healthy children. That is a point which I emphasized in my paper and I agree with Dr. Pusey that, while we cannot assure them of healthy offspring, the fact, remains in the absence of all symptoms for many, many years that such patients remain well. I do believe, however, that a negative Wassermann gains in value with each successive test and that there comes a time when we should take upon ourselves the responsibility of saying that the patient is well. This, therefore, must remain a difference of opinion between us.

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APRIL.

Editorials

THE USE OF IODINE IN SURGERY.

In 1905, Senn¹ and Kinnaman² came to the following conclusions regarding the antimicrobial and antiseptic properties of iodine:

1. Iodine is the safest and most potent of all known antiseptics.
2. Its germicidal power is far superior to that of bichloride of mercury, the acknowledged leader of all other antiseptics.
3. It approaches nearly to the ideal antiseptic.
4. A 0.5 per cent. solution is amply strong.

The rise and fall in the repute and confidence of therapeutic agents on the part of the profession are subjects of deepest interest to every progressive student. Only too often the claims made for a remedy in the treatment of certain diseases are not substantiated when subjected to an impartial trial by a scrutinizing profession. And so in regard to iodine we are commencing to note here and there a lack of confidence in regard to its antiseptic properties and find some recommending the abandonment of its use in surgery. Personally we are inclined to resent such suggestions as we are strong in our faith in iodine and while we admit that iodine is not always a perfect antiseptic agent in every instance, yet we feel that it is still entitled to being credited as our ideal antiseptic and when properly used it will give us most satisfactory results not obtainable by other measures.

1. Surg. Gynec. and Obst. Vol. 1 No. 1.
2. Journ. A.M.A. July 1905, Sept. 1905.

Too often the iodine method is blamed for resulting infection when in reality the untoward results was due to a faulty technic. The iodine preparation technic must be rigidly observed and when the entire chain is maintained intact we have never regretted placing our faith and reliance in iodine during the past ten years.

The most common errors that may be observed in its use is the shaving and cleansing of skin with soap and water, immediately followed by the application of the iodine. If the field of operation requires cleansing and shaving in such a manner this should be done at least two hours before the immediate operative sterilization with iodine. The reason for this is that water causes a swelling of the epithelium and prevents the penetration of the iodine and thus the destruction of deep seated bacteria and their spores is not accomplished. If emergency prevents the observation of this precaution then the shaving is to be accomplished without the use of water. Again, iodine that is older than a week should not be used because its strength is reduced by evaporation on account of its volatility. The objection has also been raised that blistering often results. We have never experienced such an incident and attribute its absence to a careful technic.

The technic employed is that of Bastianelli, of Rome, and is as follows:

The field of the operation is cleansed and shaved the afternoon previous to the morning of the operation and all soap is thoroughly removed by copious bathing with as hot water as can be born and then washed with ether. When brought to the operating room the field is scrubbed—not lightly gone over—with C. P. Benzine containing iodine crystals in the strength of 1 to 1000 (Solution 1.) When this solution has dried the skin is freely painted with a fifty per cent. alcoholic solution of the tr. of iodine (Solution 2) which is allowed to dry thoroughly; the field is now considered properly prepared. In emergency work the same technic is employed except that the shaving is done *without* soap or water. The solutions are made fresh each week and are kept in glass stoppered bottles.

Of 5835 surgical operations performed in the Mayo Clinic in 1912 there occurred 111 infections. If this number of infections occur in a clinic so well regulated as is the Mayo's it is not to be wondered at that we, who are compelled to operate under less favorable conditions and environments and with frequently changing assistants, should experience an occasional infection in spite of a rigid observance of those measures employed to guard against it. It, therefor, little behooves us to immediately credit the blame to iodine, rather should we seek elsewhere for the exciting cause.

Until we are possessed of reliable data demon-

strating the unreliability of iodine as an antiseptic agent and as long as our personal experiences continue to be as satisfactory as they have in the past we feel that we will be inclined to resent all efforts calculated to discredit the value of iodine. At present we feel that the critical spirit rests solely with those who have failed to employ the entire approved technic or, are seeking new and other methods to satisfy their roving, restless temperaments that impel them to cast about for something more recent and "more modern" though actually less reliable. However, we invite a free discussion of this subject.

THE COUNCIL ON PHARMACY AND CHEMISTRY.

The editor acknowledges receipt of the 1914 edition of "New and Non-official Remedies," issued by the Council on Pharmacy and Chemistry of the American Medical Association. In connection therewith we are taking this occasion to state that of all publication this book should be on the desk of every member of the profession. It is a compendium filled with valuable information regarding many medicinal preparations of proven value, reliability and therapeutic potency; further, it enables one to judge as to the worth of any preparation and enables the doctor to distinguish them from the host of utterly useless, non-potent and quack nostrums with whose literature every physician's mail is daily flooded. This book may be secured by remitting twenty-five cents to the Secretary of the Council on Pharmacy and Chemistry of the A.M.A., 535 Dearborn Ave., Chicago, Ill.

Each passing year demonstrates more forcibly the wisdom of the plan that inspired the establishment of this Council. It is difficult to estimate the good it has accomplished for the sole benefit of physician, druggist, pharmacist and manufacturer. Maligned, opposed, restrained and hampered on various sides, the Council has persistently and diligently continued its work and has imparted to the profession "The Truth About Medicines." Truths, indeed startling at times, which have cleared the haze of fraud, deception and unreliability as well as worthlessness that surrounded many of the preparations that were being manufactured and advertised as possessing therapeutic possibilities that were wholly unwarranted and unreliable. The good has been culled from amongst the worthless and bad and he who desires may now readily secure trustworthy information that will enable him to determine what are and what are not potent agents. No longer are we compelled to depend upon the manufacturer's or detail man's statement. This book supplies the requisite information. Secure it.

Speaking of "Detail-men"—we have been accustomed for the past two or three years to greet each such person presenting a new preparation with the question: "Is it approved by the Council?" This was the first requisite to secure our time and attention and no time is wasted in listening to any claims made for any preparation that does not possess the Council's approval. We feel that any preparation of intrinsic merit may readily receive a favorable report if it but complies with the rules of the Council. The manufacturer can no longer afford to ignore the Council and the physician cannot well afford to prescribe any preparation that has not been submitted and approved. This statement will be refuted by the representative that calls upon you and when he does just draw his attention to this letter which we have extracted from the *Journal of the A.M.A.* in the issue of March 14, 1914:

"To the Editor—Detail men as a class have a rather poor opinion of physicians they visit. This may not appear in the regular monologue but it always comes out on cross-examination. If you stop a detailer in the middle of his rime and put a query of your own, he soon shows how little he knows about the subject he is trying to teach, and how much less he thinks you know about it.

If you timidly mention a report of the Council on Pharmacy and Chemistry which differs in any particular from the data handed out by the monologist, he never hesitates to tell you bluntly of what a parcel of pikers the Council is composed. The secretary of the Council, who signs these ridiculous reports on proprietary preparations, is merely trying to satisfy a personal grudge which it seems the secretary has long nursed against various and sundry proprietary manufacturers! So a Mulford representative recently complained; also a Salhepaticolite.

Looking back over several years, I recall but one thing a detail man ever told me which was worth the time given him. That was a secret imparted by a Glycothymoline agent.

This Glycothymoline man was so jovial and good natured that it was utterly impossible to show him the palms of my hands. And besides, he started right off the bat to put me down for several extra pint bottles to follow up the good work he hoped I would do with the dozen small sample vials, each with the name blown in the glass to insure the doctor against substitution by unscrupulous druggists—though just how the u. d. was to effect the change between the doctor's office and the patient's hands the agent did not take time to explain. In fact his talk was very much like this paragraph—rambling on and on, without a pause for breath or interruption, until you hardly know at the end just what was said at the beginning, and before you can collect the thread of thought the agent is off again on another long tack and you trailing after him like a bather on a plank towed by a speed boat.

But at last the agent choked on a long word, and while he paused for a fraction of a second to clear his throat I seized the opportunity and remarked that I never prescribed things with the name blown in the bottle, nor had I any need for Glycothymoline. The National Formulary furnished me a perfectly satisfactory preparation in cases which needed an alkaline wash.

This was quite a long rejoinder for a doctor

to make in such an interview, I am well aware, but you see the man was almost choking and he could not stop me as soon as he would have liked. Presently, however, he swallowed that long word and raised his admonitory index-finger.

"Ah, but that's just the trouble with the N. F. imitation, Doctor," he declared. "That's just the trouble. I'm glad you brought that question up. The N. F. imitation isn't alkaline at all—it's acid, irritating. I know, because I worked in a drug-store myself and I've made gallons of the N. F. stuff—barrels of it, and it's acid, irritating. Now our product—"

"No, No," I shouted, gathering all my available strength and catching the agent on the end of his wind, "No, I've prescribed it and know it's alkaline, and not irritating."

But the agent, like the old lady's companion in the Mother Goose book, simply would not get over the stile, so we decided to test the thing. We got some red litmus paper and a bottle of Liquor Antisepticus Alkalinus, N. F., which I happened to have in the office. We thrust the red litmus into the solution and got the most beautiful reaction—the bluest detail man I ever saw.

"Well, that's one on me," he admitted after a long and alarming silence. "I'll admit I'm in wrong. But our product has a purer alkalinity anyhow."

"Purer nonsense!" I replied. "Now you're sparring for wind, aren't you, really?"

Then the agent gave up. "Doctor, I'll say this much," he confided as we shook hands. "Most of the doctors I call on swallow most anything a man says. I'm darn glad they ain't all so particular! Good-by!"

And the moral: Why is a detail man anyway?

WILLIAM BRADY, M.D., Elmira, N. Y."

Why is the detail man? We don't know and further we do not care for our time is not at his disposal unless he is supplied with recognized credentials for his preparations. For this conservation of our time we acknowledge our indebtedness to the Council and feel that it is meriting the support of the profession of Michigan—start right by securing a copy of New and Non-official Remedies.

Editorial Comments

The pernicious practice of "fee-splitting" would soon be eradicated in this state if the management of the various hospitals throughout Michigan would adopt the course of the Board of Trustees of the Grace Hospital in Detroit as outlined in the report of this Hospital appearing in the columns of the Society News in this issue. If every hospital board denied the privileges of their hospital to every surgeon guilty of the secret division of fees, and permitted only those who refused to be parties to such commercial transactions and solicitors for surgical and consultation cases to use the hospital equipment, this evil would soon become extinct.

We trust that every hospital board in the state will give this matter their serious consideration.

As this edition goes to press there remain in our drawer, which we utilize for filing original articles, but two papers for publication in our May number. Hence we are flying a signal of distress.

The *Journal* is running on an average of ten original articles in each issue. This means one hundred and twenty original articles a year. Surely our State, containing 4000 physicians, is capable of supplying its official publication with one hundred and twenty high grade, instructive, practical and valuable original articles, and not cause your editor to go begging for copy. We are confident that you will immediately respond to this call and so obviate our sending out our May number with but two original articles.

Are your society meetings being reported in our columns? If not will you not endeavor to see that provision is made at your next meeting to the end that your society meetings will be promptly reported in the succeeding issue of *The Journal*?

The movement to guard the citizen of tomorrow in the child of today, the movement to make our children strong in body while we make them strong in mind, the movement to protect the poor in their right to sunlight, the movement to make our government more full of care for the weak while not unresponsive to the right of the strong, the movements which have produced playgrounds, bathing pools, vocational schools, good government clubs, non-partisan municipal politics, wherever these movements have gained momentum and have expressed themselves in a richer community life, there has that spirit asserted itself which is characteristic of the true physician of today, and his presence as well as activity has revealed itself on every such occasion. Our profession has recognized and grasped these golden opportunities and acquitted itself with glory and becoming dignity to its everlasting honor.

Every change in society is the product of an interplay of forces, as men rarely act from simple motives, so likewise, do social forces rarely express themselves in single movements.

The up-building of efficiency and the reinforcement of character—this is at once the true meaning and purpose of organized medicine. It will strengthen us to meet the largest responsibilities of our lives. It will make us fit for greater accomplishments. The wheel of medicine has ever turned modestly. We who are the cogs of the wheel delight in the music

of its turning. May we never be unmindful of our responsibility.

The *Journal* is costing 24 cents per copy, or \$2.88 per year of 12 issues per member. Deducting your dollar paid for subscription the deficit remaining of \$1.88 per member must be defrayed by the revenue derived from our advertising sales. Unless the advertising space is a profitable investment for the advertiser he will refuse to purchase it, and to avoid bankruptcy we will have to cut down our expenses by sending you a smaller, less expensive publication. You can avoid compelling us to adopt this latter plan by patronizing our advertisers and telling them why you are doing so. Let's all boost together and thus satisfy advertiser, reader and publication committee—profit sharers from such a boosting propaganda.

The reader is referred to our correspondence column and the letter of Dr. Walter R. Parker of Detroit relative to the work that is being undertaken by the Committee on Conservation of the Vision of the A.M.A. The importance of this work is sufficient to merit the co-operation of every county society. Dr. Parker is desirous of your earnest individual and collective support.

In our correspondence department will also be found a letter describing the establishment and purpose of the Medico-Legal bureau of the A.M.A. Such a bureau is bound to be of distinct service to our members, and its establishment is but another direction in which the A.M.A. is advancing the interests of the in-

Deaths

Dr. J. B. Egglestone.—Aged 63 years, a member of the Democratic State Central committee for 20 years and chairman of the Lapeer County Democratic committee for 12 years, died suddenly at his home Feb. 19 at Imlay City. Dr. Egglestone, one of the most prominent physicians in Central Michigan, was active in Democratic politics for many years and was postmaster at Imlay City during Cleveland's first administration. He was stricken with convulsions on Tuesday and did not regain consciousness.

Dr. Egglestone was born in Wentworth coun-

ty, Ontario, May 16, 1851, the son of Harris and Elizabeth Egglestone. He received his early education there and later entered Trinity college. He was graduated from Toronto College of Medicine in 1879 and after a few months as resident surgeon at Guelph hospital came to Imlay City.

He had held almost every office in Imlay City, serving several terms as president of the village since his term as postmaster. He was married in 1883 to Miss Jennie Handley of Imlay City. Besides his wife he leaves three daughters, Mrs. Richard Loveland of Jackson, Mrs. Tom White of Lapeer, and Miss Phyllis Egglestone who lives at home.

Dr. Egglestone was in Flint on Saturday last and spent the afternoon with Hon. E. O. Wood.

Dr. Egglestone was well known and the news of his death will be received with profound sorrow.

Dr. G. W. Nafe.—On February 24th, 1914, Dr. G. W. Nafe was found dead in his office. The doctor had been in ill health for over two years and had but recently recovered from an illness of four weeks. The cause of death was myocarditis.

He was the oldest practitioner in Newaygo County, having been located at Fremont for about forty years, and up to two years ago had a very large practice. Ill health, however, had compelled him to give up most of his work during these two years.

He was prominent in politics, being a staunch Democrat. He was a member of the State Board of Registration, and had been president of the State Eclectic Society several times. He is survived by a wife and two children.

Correspondence

Philadelphia, Pa., March 13, 1914

Dr. F. C. Warnshuis, Secretary-Editor,
Michigan State Medical Society.

Dear Doctor:—

On resuming my work to a certain degree after a long illness, I find your letter of last fall, saying that I was elected an honorary member of the State Medical Society at the last meeting. Please express my appreciation of the compliment and believe that I regret the long delay in replying to your notification.

Yours truly,
JOHN B. ROBERTS.

Detroit, Mich., February 24, 1914.

F. C. Warnshuis, M. D., Sec'y. Michigan State Medical Society, Grand Rapids, Mich.

Dear Doctor Warnshuis:—

I have recently been made a member of the committee on Conservation of Vision, of the American Medical Association, to represent the state of Michigan. The idea is to appoint lecturers in different parts of the state, the material for the lectures being furnished by the American Medical Association. I shall take up the details of this work very soon, and will send you an outline of the plan as worked out by the Committee. In the meantime, I wish you might insert a personal in your journal to the effect that I have been given this appointment, in order that my communication may be received with authority.

Yours very truly,

WALTER R. PARKER.

Chicago, Ill., February 20, 1914.

Dr. F. C. Warnshuis, Grand Rapids, Mich.

Dear Dr. Warnshuis:—

The Council on Health and Public Instruction of the American Medical Association, has established a medico-legal bureau for the purpose of collecting, arranging and studying all of the available material, bearing on medico-legal questions of interest to physicians, or relating to public health matters. This bureau is in charge of Mr. John D. Hubbard, a graduate of the Northwestern University School of Law. We desire to secure all available material, bearing on medico-legal subjects, especially all pamphlets, bulletins, monographs, circulars, legislative bills, laws, reports, or special articles on any medico-legal or public health topics. As rapidly as material can be secured and studied, we hope to furnish information to all those interested on any topic coming within range of the bureau. We shall greatly appreciate it, if you will kindly send us, at any time, any such material that may come into your hands. This will be properly classified, catalogued, and preserved for use in answering inquiries on any medico-legal question. We hope to make this bureau of service to the officers and members of the state associations, members of committees on legislation, executive officers of state boards of health and medical examining boards and any others interested. Any assistance or contributions will be appreciated and of great assistance in carrying out the plans of the bureau.

With cordial thanks for your many courtesies in the past and hoping that we may, through this bureau, be of some assistance to you in the future, we remain,

Very truly yours,

FREDERICK R. GREEN, SECRETARY,
Council on Health and Public Instruction.

Muskogee, Okla., March 4, 1914.

Dr. Frederick C. Warnshuis, Editor.
Grand Rapids, Mich.

My Dear Doctor: Believing that a few scattered flowers along our path while we are here is productive of more good than many where we happen to be hereafter, wherever that may be, prompts me to congratulate you on the splendid appearance of your March issue, not only from the standpoint of mechanical excellence, which appears to me to be second to none published, but also for the very high merit contained in its reading matter. May your shadow be with us for a long time that your good work may continue.

Faternally,

C. A. THOMPSON,

Editor *Journal Oklahoma State Medical Association*.

State News Notes

About 100 members of the middle-west section of the American Rhinological Laryngological and Otolaryngological society held a meeting in Detroit on Feb. 23rd. Clinics were held in Harper Hospital; the afternoon was devoted to the reading of papers and discussions and in the evening a dinner was served at the Wayne County Medical Building.

Dr. R. L. Dixon, Lansing, Dr. J. B. Munson, Traverse City, Dr. C. B. Burr, Flint, Dr. A. M. Barrett, Ann Arbor and Dr. John L. Burkhart, Lansing, have been named by Governor Ferris as delegates to the third annual meeting of Alienists and Neurologists to be held in Chicago July 14 to 18.

The Social Welfare Association of Grand Rapids has appointed the following Consulting Medical Staff; Drs. B. R. Corbus, A. M. Campbel, H. Vandenberg, F. C. Warnshuis, R. D. Joldersma, John Hastie, Wm. Northrup, A. V. Wenger, Ferris Smith and C. E. Hooker.

Dr. and Mrs. F. J. Gibson and Dr. and Mrs. G. E. Winter of Jackson have sailed for the Mediterranean en route to Vienna where the doctors will engage in post-graduate work for the next three months.

Dr. G. A. Bulson of Jackson has returned after spending several months at the clinics in Vienna and has opened an office in the Shurley Building, in Detroit. His practice is limited to diseases of the eye, ear, nose and throat.

Dr. Angus McLean of Detroit has accepted the appointment tendered him by Governor Ferris as member of the Detroit Board of Health to succeed

Dr. J. B. Kennedy whose term of office expired on March 1st.

Dr. George L. Streeter, professor of anatomy and director of the anatomical laboratories in Ann Arbor has been tendered the position of professor of embryology at Johns Hopkins university.

Drs. Lewis W. Toles and Earl J. McIntyre of Lansing have been elected president and secretary respectively of the Board of Control of the Ingham County Tuberculosis sanitarium.

Twenty members of the Ingham County Medical Society gave a luncheon recently to Drs. J. A. Post and George E. Ranney, the deans of the medical profession in that county.

Dr. E. Mauer of Kalamazoo has completed his term of service in the Kalamazoo state hospital and departed for a year of advanced study in Europe.

Dr. Thomas H. Oliver of Battle Creek was fined \$250 and sentenced to serve ninety days in jail for the illegal sale of heroin.

Dr. William J. Duff has been elected health officer of Port Huron and has assumed the duties of his new office.

Dr. John T. Bird of Pontiac who has been seriously ill with blood poisoning in a Detroit hospital has returned home and is reported as fully convalescent.

Dr. Harold Hurley, house physician in the city hospital of Jackson has resigned from that position and is now engaged in private practice in Jackson.

Dr. G. E. Gallen of Hancock has returned after a month's absence attending clinics in New York and Boston hospitals.

Dr. Sherman Gregg of St. Joseph has accepted the appointment as assistant to Dr. G. F. Inch of the Kalamazoo state hospital.

Dr. Levi W. Gardner of Harbor Springs has resigned as a member of the U. S. examination board of surgeons.

Dr. R. I. Busard of Muskegon is suing L. C. Walker for \$15,000 for personal injuries sustained as a result of an automobile accident.

Dr. K. C. McDonald of Holly is confined to a

Pontiac hospital by reason of a severe attack of rheumatism.

Dr. Herman Ostrander of Kalamazoo has resigned as president of the Kalamazoo Anti-tuberculosis Society.

The Detroit Chapter of the Nu Sigma Nu fraternity held their annual banquet in the Cadillac Hotel on March 14th.

Dr. Harold Kirkham of Richmond has departed for a trip through Egypt.

Dr. and Mrs. T. J. Haines of Boyne City sailed March 17th for a three months' European pleasure trip.

Dr. Edward P. Wilbur of Kalamazoo has returned from a vacation spent in Florida.

Dr. M. A. Mortenson of Battle Creek has returned from a European trip.

Dr. John Pedden of Petoskey has recently been appointed as county physician.

The following program was carried out at the Hillsdale County Good Health Week. Movements similar to this one might well be started throughout the entire state:

PROGRAM.

Sunday Evening, March 15, at 7:30, M. E. Church
Rev. C. S. Wheeler, Chairman

Music—College Men's Glee Club.
"Crime Against the Boy" (for men and boys only)—Dr. A. S. Warthin, Prof. Pathology, U. of M.
Music.

Presbyterian Church

Mrs. J. W. Mauck Presiding

Music—College Girls' Glee Club.
"Sex Hygiene" (for women and girls only)—Dr. Elsie S. Pratt, Physician to Students, U. of M.

Monday Afternoon

Hillsdale Woman's Club, Mrs. F. W. Elliott, Pres.

Music—College Men's Quartette.

"Public Health Nursing"—Miss Jane M. Pindell, Supt. Training School for Nursing, U. of M.
Vocal Solo—Mrs. Waldron Stewart.
Subject Selected—Dr. A. S. Warthin, U. of M.

Monday Evening, at 7:30

Mayor L. A. Goodrich

Music—High School Girls' Chorus.

Vocal Solo—Miss Flo Gosma, College.

"Sanitary Conditions in the Philippines, China and Japan"—Dr. John Burkhart, Secretary State Board of Health.
Chorus.

Tuesday Afternoon, 1:00

County Ministers' Association in M. E. Parlors.

"The Moral Obligation to be Well"—Dr. V. C. Vaughan, Pres. American Medical Association.

Tuesday Afternoon, 2:30

Twentieth Century Club, City Hall

Mrs. Nelson Wolcott

Piano Solo—Mrs. A. T. Davis.

"Mother, Home and Baby"—D. E. McClure, Assistant Secretary State Board of Health.

Vocal Solo—Mrs. Dorothy Ruth.

Tuesday Evening, at 7:30

Dr. W. H. Sawyer

Piano Solo—Miss Marie Steele, Lansing.

Vocal Solo—Mrs. Arthur Shepard, Litchfield.

"The Doctor's Dream"—Dr. Victor C. Vaughan, U. of M.

Piano Solo—Miss Vivian Lyon, College.

"Guarding the City's Health"—Dr. Guy L. Kiefer, Pres. Michigan State Medical Society.

Wednesday Afternoon, 2:30

W. C. T. U., Mrs. H. H. Rood, President

Vocal Solo—Mrs. Dorothy Ruth.

Devotionals—

"Health and Heredity"—Dr. A. M. Barrett, Director Psychopathic Hospital, Ann Arbor.

Wednesday Evening, at 7:30

Judge F. H. Stone

Music—High School Orchestra.

"Danger of Light Cases of Communicable Diseases"—Dr. A. W. Scidmore, President State Board for Nurses.

The Scotch Quartette—Mrs. Dorothy Ruth, Mrs. Waldron Stewart, Mr. Waldron Stewart, Mr. A. T. Prideaux.

"The Tuberculosis in Childhood"—Dr. Herbert M. Rich, President Tuberculosis Association, Detroit.

"Public Health a Real Business"—Dr. R. L. Dixon. Quartette—

Thursday Afternoon, 2:30

The Thursday Club, Mrs. B. H. Bump, President

Music—

"Sanitary Conditions in Michigan Cities and Villages"—Dr. Henry F. Vaughan, Sanitary Engineer of Detroit.

Discussion—Prof. E. D. Rich, State Sanitary Engineer.

"Recent Advance in Public Health Work"—Dr. Don M. Griswold, Bacteriologist, Detroit Board of Health.

Thursday Evening, 7:30

Secretary Forrest P. Knapp, County Y. M. C. A.

Violin Trio—Mrs. Woodhams, Miss Griffith, Miss Helen Goodrich; accompanist, Miss Elsie Eggleston.

"How to Improve the City Milk Supply"—Dr. M. L. Holm, Bacteriologist State Board of Health.

Music—

"Municipal Sanitation"—Prof. E. D. Rich.

"The Fight for Pure Food"—James W. Helme, State Dairy and Food Commissioner.

Friday Afternoon, 2:30

Clover Club, Mrs. Martha Barrows, President

Music—Mr. Hall Cramner, accompanied by Miss Vena Miner.

"What the Schools Can do to Help Build Up a Science of Health"—L. Estelle Appleton, Grand Rapids.

"Disease Prevention"—Dr. Jeanne C. Solis.

Friday Evening, 7:30

Music—Reading Girls' Band

"Sanitary Problems of Small Cities"—Mrs. Caroline Bartlett Crane.

Vocal Solo—Miss Flo Gosma, College.

"Public Health"—Gov. Woodbridge N. Ferris.

Vocal Solo—Prof. E. E. Woodhams, College.

"Fakes and Frauds"—Prof. T. L. Shannon, State Analyst.

A course of special instruction for physicians engaged in psychiatric work will be given at the Psychopathic Hospital at the University of Michigan.

The instruction will be systematically arranged and will extend over a period of four weeks, beginning March 30, and closing April 25, 1914.

The instruction will be given in Clinical Lectures and Conferences, Laboratory Studies and Demonstrations and will be conducted as follows:

1. Clinical Psychiatry—Clinical Lectures Conferences and Ward Visits. 40 hours. Professor Barrett.

2. Clinical Examination Methods—Didactic Lectures and Laboratory Demonstrations. 9 hours. Dr. Haskell.

3. Serological Diagnosis and Treatment. 4 hours Dr. Haskell and Dr. Ide.

4. Neurological Clinics. 6 hours. Professor Camp.

5. Treatment of Syphilis of the Central Nervous System. 2 hours. Professor Wile.

6. Psychoanalysis and the Psychoneuroses—Clinical Lectures and Conferences. 11 hours. Dr. Reye.

7. Development of the Central Nervous System—Laboratory Lectures and Demonstrations. 4 hours. Professor Huber.

8. Anatomy of the Central Nervous System—Laboratory Lectures and Demonstrations. 20 hours. Professor Barrett.

9. Histopathology of Psychiatric Disorders—Laboratory Lectures and Demonstration. 14 hours. Professor Barrett.

For this course of instruction a fee of \$25.00 will be charged.

Applications should be made at an early date as the number admitted to the course will be limited to fifteen.

Applications and requests for information should be made to the Director of the Psychopathic Hospital.

DR. ALBERT M. BARRETT,
Ann Arbor, Michigan.

County Society News

BERRIEN COUNTY

The February meeting of the Berrien County Medical Society was held in Benton Harbor Feb. 12, seventeen members being present. Twenty-three applications for membership were received and referred to the Board of Censors.

The society unanimously adopted the following resolution: "Since indiscriminate advertising by the Medical Profession is contrary to medical ethics, disgusting to reputable physicians and suggestive of quackery, the secretary of this society is instructed to request the publishers of the various newspapers throughout the county not to give the attending physician's name when giving accounts of sickness, operations, injuries, etc."

After the business session the following program was given:

"Etiology and Pathology of Pneumonia." Dr. E. J. Witt, St. Joseph.

"Treatment of Pneumonia." C. A. Mitchell, Benton Harbor.

A general discussion followed in which nearly all present took part.

The March meeting of the Berrien County Medical Society was held at the Hotel Whitcomb, St. Joseph, March 12th, sixteen members being present. Nineteen physicians were elected to membership in the society.

A very excellent and practical paper was read by Dr. C. N. Sowers of Benton Harbor on "The Business Side of the Practice of Medicine." This aroused a general discussion which occupied the entire time set aside for the meeting, and it was unanimously agreed that the paper be sent to the editor of *The Journal of the Michigan Medical Society* for publication.

SHERMAN GREGG, SECRETARY.

BRANCH COUNTY

The annual meeting of the Branch County Medical Society was held at Coldwater January 30th, 1914. Before the business meeting a banquet was served, fifteen physicians from the county attending.

The following officers were elected for the ensuing year.

President—F. S. Legg, Coldwater.

Vice-Pres.—P. H. Gunsallus, Bronson.

Sec'y-Treas.—A. G. Holbrook, Coldwater.

Mem. Med. Leg. Com.—W. A. Baldwin, Coldwater.

Delegate—E. E. Hancock, Gerard.

Alternate—D. H. Wood, Coldwater.

A. G. HOLBROOK, SECRETARY.

CALHOUN COUNTY

The beginning of the end of quarterly meetings of the Calhoun County Medical Society occurred at their first quarterly meeting for 1914, at Battle Creek, Tuesday evening, March 3rd, when an amendment to the by-laws was presented providing for more frequent meetings. The publication of a bulletin was also mentioned, and an early appearance is anticipated. Three applicants for membership were received, and three applicants were elected to membership.

Evening meetings are proving a success, in Calhoun County and help to contribute to the interest, by making it more convenient for the members to attend.

At this meeting Dr. Alpheus T. Hafford of Albion reported a case of Myasthenis Gravis, and gave a good paper on this subject.

Our genial Secretary of the State Society was present by invitation, and aside from his usual boost-

ing of the state organization, he gave a most interesting paper, taking as his subject, Indications for Decompression.

Good fellowship prevailed in every way, and Calhoun County, Branch No. 1 proposes to be number one in every way possible from this date.

S. H. KINGSLEY, SECRETARY.

DETROIT OTO-LARYNGOLOGICAL SOCIETY

Meeting of the Detroit Oto-Laryngological Society at the Detroit College of Medicine and Surgery, January 20, 1914. Dr. J. Vernon White in the Chair.

Dr. Joseph H. Hathaway, Professor of Anatomy in the Detroit College of Medicine and Surgery, gave a lecture and demonstration of the anatomy of the nose, throat, ear, larynx and oesophagus, with many beautiful specimens.

Dr. Harold Wilson presented a patient with Vincent's agina, also a slide showing organism.

Meeting of February 17th, 1914. Dr. J. Vernon White, in the Chair.

Dr. Hugh Harrison, (as guest), read a paper entitled: A Method for Control of Inaccessible Hemorrhage. The Hypodermic Use of Alum (K₂ Al₂ (SO₄)₃).

When we refer to our text books and find page after page telling us how to control hemorrhages and then find ourselves at the bedside of a patient with all our knowledge of *Materia Medica* exhausted it is then, and only then, that we welcome any information, regardless of the source.

In September, 1913, I was called to attend a young woman 26 years of age, whose previous health had been good, but who was now afflicted with typhoid fever. Every thing went well for sixteen days. She was then taken with severe hemorrhages from the bowels, and among the many things done to arrest these hemorrhages I might mention the following: For two days large repeated doses of adrenalin morphine, tannic acid, bismuth, ergot and pituitary extract were all given, Ice bags were applied to the abdomen. The hips were elevated. In fact, I thought every available means had been used to control these hemorrhages. I can assure you that it caused me no small amount of worry to stand by and see every remedy fail. The temperature was subnormal. The pulse could not be counted at the radial artery. At the carotid it could be counted with difficulty, and averaged 150 to 160 per minute. The eyes were sunken. The abdomen was very tympanitic. A dark green fluid was almost constantly ejected from the stomach. In fact there was everything to suggest approaching death. I urged that consultation be called in order that I might have someone to share the responsibility of her death. One of our best surgeons of the city was called, and after a careful examination of the patient and review of the treatment, declared the case to be hopeless and stated that he could not offer any suggestion for further treatment which had not already been tried. At this time I suggested the use of alum hypodermatically, but my consultant would not agree to the use of it, stating that he had never heard of it being used in this manner, and strongly advised me not to try it. I consented not to do so providing that she had no more hemorrhages, but at the same time vowing to myself that I would if there was any more bleeding. In less than one hour later the nurse called me and informed me that the patient was bleeding as much as ever. Having previously discussed the mode of administration with the nurse I requested her to prepare and give it immediately. It was given in the form of a saturated

solution made by dissolving powdered alum in hot water and was injected subcutaneously. I also requested her to note carefully every change which might occur. The pulse rate just previous to administering the alum was 150 per minute and of a poor quality. In fifteen minutes after the administration of the drug the pulse rate was reduced to 130 and the quality was very much improved. In thirty minutes the vomiting had ceased, the patient had rallied considerably and declared herself very much improved. Two hours after there was a discharge of dark colored blood. The sight of this caused the family much alarm. The nurse, feeling that we could not afford to take any chances, promptly administered another dose of the alum. This also caused a marked improvement in the general condition of the patient. The pulse was reduced to 120 per minute. I saw her about ten hours later and was pleased to find that every particle of the tympanites had disappeared. Gas was freely expelled from the rectum. Fluids were then easily retained by the stomach. In fact, I will state that I do not think I ever saw a greater improvement in a patient in so short a time. Owing to the unavoidable absence of the nurse at this time a third dose was given. This reduced the pulse to 110 where it remained for several days.

The one thing which impressed me greatly was the fact that following the administration of this drug no untoward symptoms of any kind appeared, except a localized inflammation which appeared later on, at the point of administration. There was no sloughing, although considerable soreness remained for about three days. This soreness prompted me to seek the intravenous route when treating other cases. There was no feeling of fear or accelerated heart action as is so frequently noted after the administration of adrenalin.

Case Number 2. About two weeks later I was called to see a young man who had been spitting blood quite freely for the past twenty-four hours. I administered a similar dose to this patient, using the intravenous route. In six minutes the pulse rate was reduced from 101 to 84 per minute. In less than fifteen minutes the patient put his hand to his collar and remarked that he could no longer hear that gurgling within his wind pipe and the peculiar feeling in his throat had disappeared. There was no further treatment given in this case for twenty-four hours. At this time I was again called and found that the patient had been out of bed and was working about the house. He was again spitting blood. The same treatment was repeated, following which there was no further sign of a hemorrhage.

Case Number 3.—This was another case of typhoid fever which had been given all of the ordinary remedies to control the hemorrhages without avail. I advised the administration of alum hypodermatically and am pleased to state that one dose promptly controlled the hemorrhage. There was no occasion in this case to give a second dose.

A man 54 years of age, with pulmonary tuberculosis, a liver somewhat enlarged and with all of the evidences of a gastric ulcer. When called, I found him bleeding copiously from the lungs. One dose given intravenously promptly controlled the hemorrhage. Feeling that this was a case in which I could do no harm and that there would be little lost, regardless of the outcome, I informed him that it would be necessary for him to come to my office and receive daily treatment for one month or perhaps longer. During this time I administered a ten grain dose of alum intravenously each day. At the end of the first week he informed me that the sputum was very much lessened and that his breathing was much easier. The pulse rate had, as in the other cases, been much improved.

It is my opinion that these results are brought about by the fact that alum stimulates the circulatory fibres, contracts the capillaries, restores the normal tonicity of the muscles and aids materially in the coagulation of the fibrin. There are a great many other conditions in which this drug could be used hypodermatically but inasmuch as they do not come under this heading I will not mention them here.

Given intravenously there is no pain following the administration of this drug, but if for any reason it should be found impractical or impossible to use the intravenous route I would not hesitate to give it subcutaneously as in any ordinary

hyperdemic injection. I would suggest, however, if given subcutaneously that a much weaker solution be used.

Dr. Emil Amberg presented the following case reports:

1. Presentation of a patient of Dr. Ballin with a bullet (X-ray pictures) in the petrous portion of the temporal bone. The bullet had entered on the left side through the soft palate. The left eyeball protruding, hardness of hearing but no total deafness present. The labyrinth excitable, the fundus of the eye changed, etc.

2. Report of a case with presence of bacilli of the diphtheria group in the discharge from the ear and positive culture from apparently healthy tonsil. Recovery.

3. A case of emphysema of skin in a lady 27 years old caused by other party, by spraying throat after loosening tissue in tonsil removal. Duration until total disappearance about two weeks. Incidentally patient had diphtheria. Recovery.

4. A case of a baby seven months old suffering from an acute otitis media with staphylococcus aureus and Friedlaender bacillus. Three incisions in the drum on each side, whenever the temperature rose high (106°, 105.2°, 103.2°). Recovery. Discussed by N. Cooley (as guest).

5. Ear complication in possibly morbus maculosus Werlhofii. Ear affection not typical. Recovery. Discussed by Dr. R. E. Loucks, as guest.

6. A case of so-called oto-sclerosis with presence of the Schwartze symptom, but otherwise not entirely typical. May be just beginning.

Dr. Mercer presented a cast of a nose which he had operated upon for fracture.

Dr. Th. B. Cooley (as guest) spoke of an eight months old child in which he diagnosed laryngospasmus of tetany. Acute rickets present, marked cream-o tabes, general nervous hyper-excitability, Choostek's and Trousseau's signs. After chloral hydrate medication gr. I. t. i. d. the symptoms disappeared, besides authratic treatment including diet, hydrotherapy, cod-liver oil and phosphorus.

EMIL AMBERG, SECRETARY.

GENESEE COUNTY

On February 10, 1914 a meeting of the Genesee County Medical Society was held at the Masonic Temple.

Drs. Allen, Thomas, and Chandler of Flint were elected to membership in the County Society.

Following the business meetings the following program was carried out:

A paper entitled "The School Nurse and Her work" was read by Miss N. K. Keyes, of Flint.

A paper entitled "How Flint is supplied with Pure Water" was read by Mr. Roy Buzzell, who is the chemist at the new filtration plant in Flint.

Dr. Noah Bates gave a short talk on "Some Reminiscences of Thirty-two Years as Health Officer in Flint."

"Flint's Milk Supply" was responded to by Mr. Friar, the city milk inspector.

Dr. Don Knapp gave a talk on "The Relation of the Physician to the Board of Health."

On March 10, 1914, the Society held a clinic at the Home for the Feeble-Minded at Lapeer, Mich. Twenty-two Flint physicians attended the clinic. Those who were present voiced the opinion that it was the most interesting clinic that the Genesee County Society had ever held. We wish to thank Dr. Haynes for the courteous treatment that we received while there.

R. D. SCOTT, SECRETARY.

GRACE HOSPITAL, DETROIT.

The Board of Trustees of The Grace Hospital at their regular meeting, held Thursday afternoon, February 19, made numerous new appointments to the Attending Medical Staff of the Hospital. The surgical division was entirely reconstructed. Dr. Oscar Le Seure was re-elected Chief of the Surgical Department and the department divided into four divisions. The new appointments to one or other of these divisions were Dr. Herbert W. Hewitt and Dr. E. C. Hoff, Attending; Dr. R. J. Palmer, Associate; Dr. H. K. Shawan and Dr. Chas. Kennedy, Clinical Assistants. The former members of the Surgical Department who complete the department are Dr. Oscar Le Seure and Dr. Stephen H. Knight, Attending; Dr. Fred E. Thompson, Dr. Frank A. Kelly and Dr. George P. Myers, Associates. Dr. J. B. Kennedy was appointed as a member of the Medical Staff as Consulting Surgeon to the Grace Hospital.

A fourth division was added to the Department of Medicine with Dr. Albert McMichael, Attending Physician, and Dr. Harry A. Shafor, Associate Physician.

Dr. H. W. Plaggemeyer, formerly of the John Hopkins Hospital, Baltimore, was made Attending Physician to the Department of Urology, and Dr. Louis J. Goux, Attending Surgeon to the Department of Diseases of Eye, Ear, Nose & Throat.

At this meeting of the Board of Trustees an Attending Staff was elected for the new Convalescent Branch of the Hospital, located at 277 West Grand Boulevard, and known as the Miriam Memorial Branch.

This branch was opened on January 1 and these elections furnish the first attending staff for the convalescent service. Department of Medicine: Drs. Leonard F. C. Wendt, George B. Hoops, and George C. Duggan were made Attending Physicians.

Dr. James E. Davis and Dr. George L. Koessler were elected Attending Physicians in the Department of Obstetrics.

Dr. Dale M. King and Dr. R. L. Clark were elected Attending Physicians in the Department of Nervous Diseases.

The Attending Medical Staff of the Convalescent Branch by their election as such, become regular members of the Medical Board of The Grace Hospital.

Dr. George Kamperman, formerly on the teaching Staff in the Department of Medicine, University of Michigan, was elected as Attending Physician to the Department of Diseases of Women in the Grace Hospital Polyclinic. Dr. H. W. Plaggemeyer was nominated as Attending Physician to the Genito-Urinary Department of The Grace Hospital Polyclinic. With these additions The Grace Hospital Medical and Attending Staffs in all departments number seventy-five of the leading physicians and specialists of Detroit.

These additions and changes have become necessary on account of the phenomenal growth of the Hospital, from an average of seventy-five patients per day in 1904 to a capacity of 282 beds at the present time in its various departments.

For several years past the Board of Trustees have keenly recognized the necessity for increasing the bed capacity of the Hospital in its various departments as rapidly as its available funds would permit. The Board of Trustees is comprised of an active group of business men who have been in close touch with the industrial development of the city and were able to foresee a rapid increase in the demand for hospital accommodations. The Workmen's Industrial Compensation Act, which went into effect Sept. 1, 1912, also forced the Hospital to increase its number of Ward beds and greatly enlarge its accommodations for injured workmen. This enlargement has been under way during the past eighteen months so that the hospital in its Main buildings and Branches has a capacity for the care of 200 ward patients of both sexes, in addition to its private room service.

At this meeting the Board of Trustees a special effort was made towards raising the standard of Medical Ethics. The Board adopted a resolution requiring that present and all subsequent members of the various Medical Staffs of the Hospital to take a decided stand against violators of medical ethics, and especially against surgeons and physicians who drum up business by splitting fees. The entire Attending Medical Staff at a combined meeting, held Tuesday evening, Feb. 17, adopted a resolutions requesting the Board of Trustees to make it obligatory for all members of the Attending Medical Staff to sign a "Declaration" opposing the practice of fee splitting and the soliciting of surgical work as contrary to the general principle of medical and surgical ethics and the welfare of the public. This was unanimously adopted by the Medical Staff at this meeting and confirmed by the Board of Trustees, and thereby was made one of the official rules of the Hospital.

The Medical Staff is headed by the following men, who comprise the Executive Committee and

who are responsible largely for the numerous additions to the Staff that have been made in the past few months: Drs. Oscar Le Seure, Stephen H. Knight, Harold Wilson, Geo. G. Caron, Harlow B. Drake, Rollin H. Stevens, W. L. Babcock.

The Board of Trustees of the Hospital are as follows: Messrs. Truman H. Newberry, H. Kirke White, Philip H. McMillan, George M. Black, Henry E. Bodman, Hamilton Carhartt, M. T. Conklin, Chas. A. Dean, John S. Newberry, Wm. T. Barbour, Dexter M. Ferry, Jr., Gaylord W. Gillis, Henry B. Joy, James S. Holden, James H. Flinn, Henry M. Leland, and Hon. Don M. Dickinson.

ADVANCE SHEETS OF THE ANNUAL REPORT OF THE GRACE HOSPITAL FOR 1913.

Total number of patients treated in Hospital during 1913	5647
Total number of days' treatment furnished patients in Hospital	75,804
Daily average number of patients for the year 1913	202
Average length of treatment of each patient, days	13½
Cost of maintenance per patient per day	\$ 2.56
An increase of 21 cents per patient per day over last year.	
Total hospital expenses for 1913 were	\$194,204.90
Total Hospital earnings for 1913 were	176,143.69
This deficit was made up in part by the income from the general endowment funds.	

Of the 5647 patients treated, 3567 were admitted to wards, 1431 to private rooms and 648 to semi-private accommodations.

On account of the rapid industrial development of the city the demand for moderate priced ward accommodations has increased to a greater extent than the hospitals can meet with their present endowments.

CHARITY WORK OF THE HOSPITAL.

Number of days' treatment furnished patients in the hospital free of charge	14,934
Number of visits to medical, surgical and dental departments of the Polyclinic free of charge	10,387
as compared with 5979 during 1912.	

This is an increase of 4408 visits or 73.7 per cent.

The demands on the Hospital for free treatment and care of indigents increased in all departments during 1913.

From the free dispensary 419 patients were transferred to the Hospital for in-treatment for periods ranging from one day to six months. Of this number 378 were treated in the Surgical, Eye, Ear, Nose and Throat, or Gynecological Departments and relieved by surgical operations.

SOCIAL SERVICE DEPARTMENT.

The work started March 21st, 1913. The following statistics cover the work carried out from its inception, March 21st, 1913 to Dec. 31st., 1913.

652 visits were made to the homes of patients who attended the Clinic, also city, country and charity patients discharged from the Hospital.

- 12 cases were reported to the Jewish Charities.
- 31 cases were reported to the Associated Charities.
- 21 cases were reported to the Baby Milk Fund Society.
- 13 cases were reported to the Visiting Nurse Association.
- 5 cases were reported to the Tuberculosis Society.
- 1 case was reported to the Juvenile Court.
- 6 cases were reported to the St. Vincent De Paul Society.
- 10 cases were reported to the Board of Health.
- 2 patients without homes were sent to Eloise.
- 3 patients were reported to the Society for the Prevention of Cruelty to Children.
- 3 children were placed with the Michigan Children's Home Finding Society to be cared for while the mother found work in the Hospital, the father having deserted the family.

Work was found for 15.

33 women and children were sent for summer outings through the kindness of the Associated Charities, the Michigan Fresh Air Society, and the Free Press Camp.

59 patients were refused free clinic care and sent to private physicians, it having been found that their circumstances enabled them to pay for medical care.

The work of this department demonstrates the necessity for active social work among families who are under stress during illness or indigent and among convalescent ward patients who are discharged from the Hospital. The Hospital Social Service Worker has spent the greater part of her time during the past year between the Hospital and homes or rooms of dispensary and ex-in-patients.

BEQUESTS AND DONATIONS RECEIVED DURING 1913.

Mrs. Helen H. Newberry.....	\$20,000.00
Mr. Truman H. Newberry.....	
Mrs. H. B. Joy.....	
Mr. John S. Newberry.....	

For the endowment of a private room for the use of the graduates of The Grace Hospital Training School for Nurses.

Mrs. Helen H. Newberry, bequest of \$5,000.00, the income of which is to be devoted to the maintenance of the Helen Newberry Nurses' Home.

Mrs. E. W. McGookin, contribution for the purchase of sterilizers for the lying-in department.

Board of Lady Managers, The Grace Hospital \$225.00

In partial payment of the salary of the Hospital Social Service Director.

Mr. Henry M. Leland, contribution to Social Service fund.

Mr. W. T. Barbour, contribution to Social Service fund.

MIRIAM MEMORIAL BRANCH.

This property, located at 261 to 263 West Grand Boulevard, was opened as a convalescent and maternity branch on January 1st, after being completely remodeled to accommodate these patients. It was donated by Mr. and Mrs. H. M. and W. C. Leland, and has been designed and equipped to care for 40 patients. It is a veritable miniature hospital and is complete in all its appointments. Plans have been made to manage the hospital directly from the main group with a local supervisor in charge.

EMPLOYES' BUILDING.

On September 1st the Trustees of The Grace Hospital appropriated \$45,000 to build and equip a home or apartment house for domestic employees. Designs and specifications drawn by Albert Kahn were already on hand, contracts were let and the building constructed in an exceedingly short time. It is now nearing completion and will be ready for occupancy in March. It is located on Alexandria Ave., facing Brush Boulevard.

DECLARATION.

I hereby promise upon my honor as a gentleman that I will not, so long as I am a Member of The Grace Hospital Medical Staff, practice division of fees in any form; neither will I submit bills for others referring patients to me; nor will I permit them to submit bills for me; nor joint fees with physicians or surgeons referring patients to me for operation or consultation; neither will I in any way, directly or indirectly, compensate any one referring patients to me; nor will I utilize any man as an assistant as a subterfuge for this purpose. I furthermore agree to studiously avoid visiting, treating or advising the patient of another physician without his knowledge or consent; and furthermore agree to maintain in my relations with other physicians the highest recognized standard of Medical Ethics, whether in consultation or in hospital work.

W. L. BABCOCK, M.D.

GRATIOT COUNTY

The first quarterly meeting of the Gratiot County Medical Society was held at the court house in Ithaca, on Thursday February 26th, 1914. The program was carried out in full.

The discussion of Doctors Barstow's, Thornton's, and Gardner's papers precipitated a long discussion on the question of reimbursing the doctors for the care of the poor, by the Board of Supervisors. Dr. McLean was called on to explain what is known as the Tuscola County plan. Dr. Barstow advocated what is known as the Hillsdale County plan. On motion of Dr. Barstow, President Monfort was requested to act as Chairman of a committee of Ithaca physicians, and with as many others as he thought best confer with the Board of Supervisors regarding the care of the poor.

Dr. Pankhurst then read his paper on the use of Bacterial Vaccines, which was enjoyed by all, but because of the lateness of the hour discussion was limited and on motion of Dr. Gardner. Dr. Pankhurst was given a vote of thanks for his excellent paper. Dr. Weller then read his paper on Puerperal Eclampsia as encountered by the country practitioner. Many were ready to discuss this excellent paper, but the time being limited it was moved that the Doctor's paper be sent to the State Journal for publication.

The meeting then adjourned to the dining room in the basement of the courthouse where an excellent supper was enjoyed by all at the expense of the Ithaca physicians. All were agreed that this was the best meeting of the Society that has been held at Ithaca in a long time.

E. M. HIGHFIELD, M.D., SECRETARY.

KALAMAZOO ACADEMY

Tuesday, February 24, 1914 at 1:30 p. m.

Payment of Dues—Treasurer, Dr. Frances Elizabeth Barrett, 1130 S. West Street.

1. Business Meeting.
2. Case Reports.
3. (a) Mental Deficiency.

(b) Minnesota Colony System for the Care of Epileptics. Dr. A. C. Rogers, Faribault, Minn.

Discussion by—Drs. R. L. Dixon, Lansing; A. I. Noble, W. A. Stone.

4. Roentgen Examination of the Head. Dr. P. M. Hickey, Detroit, Mich.

Discussion by—Drs. A. W. Crane, F. E. Grant, E. J. Bernstein.

We are very glad to welcome our neighbors into our midst. Both for the good of organized medicine in general, and ourselves in particular, we should boost this society. For it is written: "No man can live unto himself alone." This is more applicable to medicine than to almost any other human activity. We regret that more medical men do not profit by the visits to our society of essayists

who put forth their best efforts and sacrifice greatly that we may feel that we are getting something.

Dr. Case gave an exhaustive lantern slide demonstration of Ileal Stasis; only thirty members were present to hear this comprehensive treatise of this subject. This is a busy time of the year, but these programs you cannot afford to miss, though you may lose some calls in and out of the office. Good things are always expensive, and it takes sacrifice to obtain them.

Dr. Wilbur reported two cases of foreign bodies in the eye at the last meeting. X-Ray plates were passed around that demonstrated the position of the foreign bodies quite accurately. He emphasized the indispensable aid of the X-Ray plate in case of injury to the eye from foreign bodies.

Though we believe the mission of the Bulletin to be that of a scientific nature to keep the absent member in constant touch with his society, we will digress somewhat from the usual routine and quote from Dr. Osler and Mr. Benjamin Jowett, for the serious meditation of the young member, and for the revival of the student days that have been crowded out by the issues of life and death, and grave responsibilities of a busy life in medicine.

"The want of energy is the main reason why so few people continue to improve in later years. They have not the will, and do not know the way. They 'never try an experiment' or look up a point of interest for themselves; they make no sacrifices for the sake of knowledge; their minds, like their bodies, at a certain age become fixed. Genius has been defined as 'the power of taking pains'; but hardly any one keeps up his interest in knowledge throughout a whole life. The troubles of a family, the business of making money, the demands of a profession, destroy the elasticity of the mind. The waxen tablet of the memory, which was once capable of receiving 'true thoughts and clear impressions,' becomes hard and crowded; there is no room for the accumulations of a long life (Theat. 194 ff.). The student as years advance rather makes an exchange of knowledge than adds to his stores."—Jowett, "Introductions to Plato."

Tuesday, March 10, 1914 at 1:30 p. m.

Reading of minutes of previous meeting.

1. The Cardiac Arrhythmias.

Demonstration of use of Mackenzie Polygraph. Lantern slides illustrating various cardiac conditions. Dr. Walter J. Wilson, Jr., Detroit, Mich.

Discussion by Dr. F. C. Penoyer, Dr. R. P. Stark.

2. Principles underlying Tendon, Fascia and Bone Transplantation. Dr. Dean Lewis, Chicago, Ill.

Discussion by Dr. R. C. Stone, Battle Creek.

1. Anesthesia. Dr. Wm. C. Huyser, Kalamazoo.

Discussion led by Dr. R. G. Cook.

2. The Orthopedic Treatment of Infantile Paralysis.

Clinic on Infantile Paralysis. Dr. John L. Porter, Chicago, Ill.

Discussion led by Drs. H. O. Statler and F. M. Ilgenfritz.

3. Reports of Cases.
4. Business Session.

Dr. Porter will give a clinic in the Academy rooms on Infantile Paralysis. This should be of supreme interest to every physician. If you now have a case, or have had one that presents some clinical phases of disease, or complication therefrom, will you kindly bring all cases to the Academy where the clinic will be held, or notify Dr. Frederic Shillito, Chairman of the Clinical Committee. The more complete the clinical history the greater the interest.

The Kalamazoo Academy has been fortunate in not having had any delinquents for 1913. Remember if your dues are not paid by April 1, 1914 your name will appear in the *Journal* as a delinquent; this will mar our good record, and you will not be a recipient of the April number of *State Journal*. Team work and "get together" will prevent such irregularities.

C. B. FULKERSON, SECRETARY.

LENAWEE COUNTY

The Lenawee County Medical Society held one of the most interesting and well-attended meetings in its history March 10th in the afternoon, hearing two illustrated lectures at the New Family Theatre, one illustrated by motion pictures of surgical operations. These two lectures were the attraction for an unusually large attendance with doctors from the city and other places in the country in attendance in large numbers. In addition to the members of the medical profession the Bixby Hospital board, nurses, members of the school board and clergy, and a small number of other prominent people of the city were present.

Preston M. Hickey, one of the leading X-Ray specialists of Detroit, lectured on the use of the X-Ray treatment in medicine and surgery. His address, illustrated by a number of stereopticon plates, was unusually interesting. The clearness and definition of the plates, showing the manner and effect of treatments, added greatly to the interest of the talk.

J. H. Jacobson, of Toledo, a leading physician and surgeon of that city, spoke on the use of local anesthesia in surgical operations. A moving picture film, showing several operations as performed by the aid of local anesthesia, was of great interest, and helped the speaker bring out the points of his talk. Dr. Jacobson was accompanied here by Dr. Todd of Toledo, who was a guest of the medical association while here.

MANISTEE COUNTY

The regular monthly meeting of the Manistee County Medical Society was held at Ramsdall Hall, with an unusually large attendance.

At 6 p. m. a very delectable luncheon was served

by our worthy "Chef" Dr. Harry J. Combs. After cigars were passed the meeting was called to order, President E. S. Ellis presiding.

The minutes of the previous meeting were read and approved.

Dr. Louis L. Ramsdall read the paper of the evening, "The Doctor and His Success." The subject was very carefully handled, considering the doctor in his relation to society, and the attitude of society towards the doctor. Also the doctor as a brother practitioner in his own profession, and in his attitude towards his patients: deducting that it's the finer human sensibilities in us that make the highest degree of success, practical ability being equal. And, while these qualities are largely born in us, yet they can be larger cultivated.

The paper was splendidly received, and it was suggested that the secretary forward same to the editor of the *State Journal* for publication.

The meeting then adjourned.

DR. LEE A. LEWIS, SECRETARY.

MARQUETTE—ALGER COUNTY MEDICAL SOCIETY

The February meeting of this society was held in Marquette on the evening of February 16th. As there was no prearranged program the new President, Doctor C. J. Larson, of Negaunee, opened the session with a talk on the "County Medical Society." He said in part: Every County Society seems to have a common life history—an enthusiastic birth, a more or less stunted growth and then renewed vitality and great development. Numbers alone do not count for everything, for some national societies of high efficiency can at some meetings muster only ten or a dozen members. What is needed most of all is an "*esprit de corps*" permeating the whole organization an enthusiasm which grips every member and compels him to perform gladly any duty which the Society may request of him; a receptive state of mind that he may note what the various speakers affirm and decide by his own investigations of the subject whether they have read their theme aright, and the criticism which may follow, even if severe, need not be given in a malignant spirit. Again every Society desires as members every eligible man in the County and we hope to have that duty done before the state solicitor comes around. The conditions as printed on the application blanks are liberal enough in all conscience. It is a mistake for any man to think that he can stand alone in the exigencies of practice. The field is too broad, the knowledge is too deep, and the ability of most minds to retain and apply all they seek to know too limited, and at the bedside one finds that the symptoms are baffling and the judgment fallacious.

No, one man knows it all and each one needs the moral support of the county society, and the county society needs him. One says to me "I don't go to the meetings because I can read all they have

to say in the books." It is very true that you busy men are not engaged in research work and still there is not one of you who is not intensely interested in all the research work as reported in your medical magazines and books. You pride yourselves upon being up to date. Why, gentlemen, there is enough "medical news" in sight at the present moment to keep us all taking medicine for the next twenty-five years. Get on your feet once in a while and tell us what you know, what you expect and what you hope about these things and the society will flourish like a green bay-tree.

SAGINAW COUNTY

The regular monthly meeting of the Saginaw County Medical Society was held at the City Hall Feb. 26th, 1914, with an attendance of about forty.

Pres. McGregor appointed the following as members of the local committee on Red Cross Medical Work of the A.M.A. The President and Secretary of the Society, Dr. H. J. Meyer, Dr. J. W. McMeekin and Dr. B. B. Rowe.

Dr. Geo. E. McKean of Detroit gave an enlightening talk on "Blood Pressure, and What It Means to the Man in General Practice."

Dr. H. J. Meyer gave a splendid and comprehensive paper on "Gastro-Enterostomy."

Several new members were elected and the County Society is now in a flourishing condition. The annual meeting will take place at the meeting of March 19th.

A. R. MCKINNEY, SECRETARY.

SHIAWASSEE COUNTY

The Shiawassee County Medical Society met in Owosso on March 3rd, 1914 in the Y. M. C. A. rooms, with a good attendance.

Pres. J. A. Rowly of Durand called the meeting to order, and introduced Dr. A. O. Hart of St. Louis, who read an interesting paper on "Vaccines and Immunity in Their Relation to Surgery." The paper was a very practical one, giving details of actual experience, and yet was not too technical for the average general practitioner. The recent advances in this line of treatment were outlined and a brief resume of the subject up to date was most interestingly made. Dr. Hart received a vote of thanks for his most excellent paper.

Dr. A. M. Hume made a fine report of the recent meeting in Chicago of the various State Boards of Registration, having represented the State of Michigan at that meeting. He assured the Society that Michigan now stands in the front rank as far as regards medical laws.

At the conclusion of the discussion of the paper and report an oyster supper was served in the dining room, to which all did full justice.

W. E. WARD, SEC'Y-TREAS.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

The fifth regular meeting of the Southwestern Michigan Triological Association was called to order by the President, Dr. E. J. Bernstein, in the Academy of Medicine Rooms, Kalamazoo, Monday, March 2nd, at 8 p. m.

The minutes of the previous meeting were read and approved as read. Dr. Bernstein presented two cases. One of ptosis of the right lid with paralysis of the oculo-motor muscles with the exception of the external rectus. This condition came on suddenly and has continued for about five weeks, showing no apparent improvement. Specific history is denied.

The other case presented was a young lady about twenty-six, a school teacher, who had a discharging ear with no pain for two weeks before consulting the doctor, whom she consulted for the removal of a polypus. The doctor, after the removal of the polypus, developed the bacillus mucosus capsulatus, and the X-ray showed destruction of the mastoid. The radical operation was done next day, at which it was necessary to carefully curette the bony canal for the facial nerve. Also to destroy the lateral semi-circular canal, the necrosis had been so rapid and so extensive. A week later, Thiersch' grafts were applied to the cavity, according to Balance' method. Immediately after the first operation was completed, facial paralysis developed. At the operation for applying the grafts, the facial nerve was inspected and found intact. At the present time, control of the orbicularis muscles and the muscle of expression is returning. Epidermization of the mastoid is complete.

Dr. F. E. Grant read a paper upon the treatment of chronic middle ear catarrh, in which he paid especial attention to the nose and throat conditions responsible and advocated in the treatment the careful correction of all these conditions, together with pneumo-massage of the drum, and the loosening or relaxation of all adhesions found. He advocated also medication of the tympanum by the Eustachian catheter. In the discussion which was participated in by Drs. Haughey, Chapman, Colver, Bernstein and Harrington, the Heath cantharidine treatment and the various instruments for the restoration or re-education of the hearing were discussed, the opinion being that these instruments accomplish but little if any more than our old armamentarium.

Dr. Bernstein presented an illustrated discussion of the submucous resection of the nasal septum. The illustrations (from Freer), and the able presentation of the subject brought out many valuable points. Special stress was laid upon the continuation of the periosteum and perichondrium from one side to the other at the junction points between bone and cartilage in deflected septum and to the over riding of bone and cartilage. A general discussion followed.

Upon vote, the next meeting will be held at Ann

Arbor with a clinic by Dr. R. Bishop Canfield.
Meeting adjourned.
WILFRED HAUGHEY, SECRETARY.

WAYNE COUNTY

Monday, March 2—General Meeting.

Anoci Association. Dr. Geo. W. Crile.

Subscription dinner for Dr. Crile, 6:30 p. m. sharp.

The man who "Dislocates Most any Joint of His Body At Will" performs before Dr. P. M. Hickey's X-Ray machine.

Last Monday night Dr. Hickey demonstrated the fact that "Dr. Whitman," to whom we all donated liberally for his performance a couple of weeks ago—*does not* dislocate a single joint. He took a series of pictures in the presence of three witnesses—all of which showed that "Dr. Whitman's" joints stayed as the Lord intended they should, and explained that his contortions were muscular.

The following account which is interesting, was published thoroughly a short time ago:

Elias Whitman, who for 20 years has been demonstrating to the medical world a puzzling, India-rubber flexibility of the various joints of his body, has gained the name of "The Man Without a Diaphragm."

Mr. Whitman contorted his chest, evidently experiencing great pain, and dropped the apex beat into the abdomen. One of the professors brought a stethoscope to bear, but said he was unable to verify the position of the organ, after the alleged dislocation, despite the fact that he was directed by Mr. Whitman.

Mr. Whitman waives aside the skepticism, and says he has ample testimony from physicians the world over who have studied him, and say that the heart is actually lowered, although none has been able to ascertain how it is done.

At the age of five years, Whitman was rushed to a hospital by his mother, who pointed out to physicians a dislocation of the shoulders. Examination showed the child to have loose ligaments at every joint. Whitman, now 25 years of age, has been touring the world, exhibiting the "freak of nature" since.

The man made six dislocations of the shoulder, four of the hips, drew the liver and intestines into the chest, made four dislocations of the spine, and allowed the sophomores to reduce the dislocation under the new Fernberg method, which was given its initial experiment at Heidelberg.

Besides skipping about with both hips dislocated, hopping from a table to the floor, and putting them to other tests. Mr. Whitman showed no hesitancy in allowing the students to work over him, trusting them with the reduction of the dislocations and directing their work.

"I am always in danger of death from the dislocation of the heart," he said. "I have been warned again and again to cease the experiment."

During the three seconds that he says he has the heart in the abdomen, the power of breathing is paralyzed, and the danger that the beating of the heart will forever be stilled, is always confronting him. He is a small, vigorous man. He does not wear an overcoat in the coldest weather, the cold, he said acting as a tonic on the ligaments and joints.

"Halle University" conferred the honorary degree of "Doctor" upon him.

Program.

Monday, Feb. 23—Surgical Section.

Practical points (of special interest to the general practitioner) in the treatment of diseases of the ear. Dr. J. M. Ingersoll, Cleveland, O.

"Tonsils in Relation to General Infection." Dr. G. E. Shambaugh, Chicago, Ill.

Monday, March 9—Medical Section.

Polio-myelitis. Wesley Taylor.

A study of Diphtheria Carriers and their Treatment. Theo. McGraw, Jr.

Monday, March 16—General Meeting.

Present interpretation of the Laboratory Diagnosis of Syphilis. H. R. Varney.

A Sero-Enzyme test for Syphilis. F. W. Baeslack.

R. L. CLARK, SECRETARY.

Book Reviews

MODERN MEDICINE. ITS THEORY AND PRACTICE. In original Contributions by American and Foreign Authors. Edited by Sir. Wm. Osler, Bart., M.D., F.R.S., Regius Professor of Medicine in Oxford University, England; Honorary Professor of Medicine Johns Hopkins University, Baltimore; formerly Professor of Clinical Medicine in the University of Pennsylvania, Philadelphia, and in McGill University, Montreal; and Thomas McCrae, M.D., Professor of Medicine in the Jefferson Medical College, Philadelphia; Fellow of the Royal College of Physicians, London; formerly Associate Professor of Medicine in Johns Hopkins University, Baltimore. In five octavo volumes of about 1000 pages each, illustrated. Volume II. Diseases caused by Protozoa and Animal Parasites—Diseases Due to Physical, Chemical and Organic Agents—Disease of Metabolism and of the Respiratory System. Just ready. Price per volume, cloth, \$5.00 net; half morocco \$7.00 net. Lea & Febiger, Publishers, Philadelphia and New York, 1914.

The prompt appearance of the second volume of the new Osler and McCrae's Modern Medicine gives evidence of excellent organization and efficient co-operation between editors and contributors. This volume has the same handsome appearance as its predecessor, and the same ex-

ceptional beauty. The subjects treated include Protozoan and Metazoan Infections; Diseases caused by Physical, Chemical and Organic Agents; Diseases of Metabolism and Diseases of the Respiratory Tract.

The eminence of the contributors and the authoritative character of their contributions make it difficult to select any for special comment. Two subjects, however, which have undergone the most revolutionary changes since the appearance of the original work, are represented by Sir William Osler's extensive article on Syphilis, in which treatment are given at considerable length, and an entirely new chapter of high authority on Pellagra. Other sections discuss subjects which have been along the recent line of advance of medical science, and make the volume of exceptional interest and value.

The reviewer needs to add but little more, because he is aware that the profession will be eager to possess this book, and thus acquaint themselves with the contents of so authoritative a work.

PATHFINDERS OF PHYSIOLOGY. By J. H. Dempster, A.B., M.D., Detroit. Published by the Detroit Medical Journal Company. Cloth, 66 pp. Illustrated.

The author of this work is well known to the profession of the state by reason of his editorship of the *Detroit Medical Journal*. The contents of this little volume is a collection of the copy that has appeared from time to time in his journal.

In an interesting and instructive way the relations and influence of certain men upon the discovery of now recognized physiological functions are described. One cannot help but profit by the reading of this book, and we congratulate the author at the same time expressing the wish that the reception accorded to this volume may inspire him to further and broader work in this field.

INFECTIONS OF THE HAND. A GUIDE TO THE SURGICAL TREATMENT OF ACUTE AND CHRONIC SUPPURATIVE PROCESSES IN THE FINGERS, HAND AND FORE-ARM. By Allen B. Kanaval, M.D., Assistant Professor of Surgery, Northwestern University Medical School, Chicago. New (2nd) edition, thoroughly revised. Octavo 463 pages, with 147 illustrations. Cloth \$3.75 net. Lea & Febiger, Philadelphia and New York, 1914.

This is undoubtedly one of the most valuable and practical books which the physician could place in his library. The frequency of injuries to the hand, the disastrous results which may occur, and the importance of proper treatment, are well known. Dr. Kanaval has made a special study of this field, and has obtained remarkable results; and his book is the only one in existence which covers its subject fully and ex-

clusively. It is the result of several years' work, comprising experimental and anatomical investigations carried on in conjunction with careful clinical observation of an extensive number of cases. By the use of the measures described in this volume it has been possible, even in neglected cases, to insure a restoration to complete function in 95 per cent of the abscesses of the facial spaces; while in tendon-sheath infections the morbidity has been reduced fully one-half, and the usefulness of many a hand that is now lost might be preserved if every practitioner and surgeon were equipped with the information set forth by Dr. Kanaval in regard to the diagnosis of this frequent and too often under-rated lesion. The practical character of this work may be shown by the following quotation from the preface: "The chapters are so grouped that the busy practitioner can find the part dealing with his particular case quickly. Given a case in which the practitioner is in doubt, he should read the chapter upon 'Diagnosis and Treatment in General.' This will indicate the group into which his case falls, and will also direct him to the proper sections of the book where cases of that nature are treated in detail." The illustrations are large and remarkably clear and instructive.

The reviewer wishes that he could draw to the personal attention of every reader the value of this volume. The grasping and applying of these principles by the practitioner will enable him to obtain results equally as good as those of the author. The book cannot be recommended too highly. It should be owned by every member of the profession.

DIAGNOSIS IN THE OFFICE AND AT THE BEDSIDE. The Use of Symptoms and Physical Signs in the Diagnosis of Disease. By Hobart Amory Hare, M.D., Professor of Therapeutics, Materia Medica and Diagnosis in the Jefferson Medical College of Philadelphia. New (7th) edition, thoroughly revised and rewritten. Octavo, 547 pages, with 164 engravings and 10 full-page plates. Cloth \$4.00 net. Lea & Febiger, Philadelphia and New York, 1914.

The great practical value of this work and its appreciation by the medical profession is shown in the demand for a seventh edition. In this new issue the size of the volume has been reduced by the omission of laboratory diagnosis, and the price has been correspondingly brought down to four dollars. This places it on the same basis of cost as Hare's *Practical Therapeutics*, to which it is an admirable companion. With these two books before him, the practitioner is well equipped for the most puzzling case. He could not have more authoritative information in a form more definite or more easily accessible.

The book is exactly what its title claims—an Office and Bedside Diagnosis. It is primarily a regional study of symptoms; and it points out clearly just what the physician should look for

from the moment he first sees his patient until a positive diagnosis is reached. It takes up each problem as the physician must take it up in the hospital ward, in the clinic or in actual practice, and by valuable tabulations points out, wherever possible, the differentiation between conditions which are similar. Thus it virtually eliminates the possibility of error. It is a striking example of Dr. Hare's wonderful ability to pick out what is essential, and present it in such a way that it will be of the utmost service. The excellence of the work is further enhanced by the series of admirable illustrations, and by the full index covering fifty pages, which makes any point in the book instantly available.

Every member of the profession will find this work a most valuable aid, and to be without it will tend to eliminate from his resources that which he cannot well afford to be without.

THE CLINICS OF JOHN B. MURPHY, M.D. at Mercy Hospital, Chicago. Volume III, Number 1. Octavo of 190 pages, 91 illustrations. Philadelphia and London: W. B. Saunders Company, 1914. Published Bi-Monthly. Price per year: Paper, \$8.00, cloth, \$12.00.

Number 1 of Volume III of the Surgical Clinics of John B. Murphy is before us—admittedly welcome. The first that attracts our attention is the editorial note that: "Beginning with the April number there will appear in each issue a detailed talk by Dr. Murphy on some special topic connected with the general subject of Surgical Diagnosis." This is bound to add to the value of the clinics, for the subscriber in a few years will have in his possession a complete series of articles on important factors requisite to reach an accurate diagnosis and which have been proven absolutely reliable in Dr. Murphy's large clinical experience.

This number is of added value on account of its containing valuable discussions by the following noted visitors who have attended the clinic from time to time: Sir Rukman J. Godlee of England; Dr. G. E. Brewer of N. Y.; Mr. Herbert Patterson of London; Dr. G. W. Crile of Cleveland.

All the cases reported contain much that is instructive and profitable. The clinics deserve a large subscription. You will profit exceedingly from them.

PROGRESSIVE MEDICINE. Volume XVI, Number I. A quarterly digest of advances, discoveries and improvements in the medical and surgical sciences. Edited by Hobart A. Hare, M.D. Price \$6.00 per annum. Lea & Febiger, Philadelphia.

Surgery of the Head and Neck by Chas. H. Frazier; Surgery of the Throat by John Ruhrah; Diseases of Children by Floyd M. Crandall; Phinology and Laryngology by George B. Wood; Otology by Arthur B. Duell, comprises the contents of Volume XVI, Number I of this publication and thereby

places before the profession the recent advances and discoveries in these fields of medicine and surgery during the past three months.

The progressive medical man will at a glance perceive the immense value of a publication sent out after having been subjected to the editorial scrutiny of such recognized authorities as have edited this number. To remain abreast and progressive implies that you are receiving this work which merits your patronage and material support.

PRACTICAL SANITATION. A handbook for health officers and practitioners of medicine by Fletcher Gardner, M.D. and J. P. Simonds, B.A., M.D. Illustrated, cloth, 402 pages. Price \$4.00. C. V. Mosby Co., St. Louis, Mo.

Here is an excellent guide for health officers, and we believe the only book of its kind. It is a plain exposition of the duties of a health officer and advances safe measures whereby he may meet any emergency that may arise. It goes into the subject of quarantine very carefully and groups the different diseases requiring quarantine. The examination of school children is covered in a practical manner as are also various plans for the prevention of diseases. No health officer should be without this work and the doctor will find it of value and assistance.

ANATOMY AND PHYSIOLOGY. A Text Book for Nurses. By John Forsyth Little, M.D., Assistant Demonstrator of Anatomy, Jefferson Medical College, Philadelphia. 12 mo., 483 pages, with 149 engravings and 4 plates. Cloth, \$1.75 net. The Nurses' Text-Book Series. Lea & Febiger, publishers, Philadelphia and New York, 1914.

This concise work presents all the essential points of anatomy and physiology, which the nurse must have at hand for the proper comprehension of her professional duties. The author's style is clear and untechnical, and no theories have been included except those which have been definitely accepted by teachers of these subjects. Emphasis has been placed on the descriptions of organs in the practical work of the nurse. The volume is extremely well organized, and the judicious use of heavy-faced type brings in their proper relations the various headings and sub-heads according to their importance. The illustrations are very unusual in their excellence; many of them are taken from Gray's Anatomy, and these have the names of the parts engraved directly on the face of the cut, so that each part, its relations and extent are manifest at a glance. At the end of each chapter there is a list of questions which serves to impress upon the mind the salient points in that chapter. At the end of the book there is a table of weights and measures, a full glossary, and an admirable index. This work stands alone in its efficiency as a teaching instrument in the nursing field.

It should be in the library of every training school. No lecturer on anatomy to nurses can afford to be without it.

DIAGNOSIS METHODS. A guide for history taking, making of routine physical examinations and the usual laboratory tests necessary for students in clinical pathology, hospital internes and practicing physicians by Herbert T. Brooks, A.B., M.D., Professor of Pathology University of Tennessee. Second edition, cloth, 82 pages. Price \$1.00. C. V. Mosley Co., St. Louis, Mo.

This is a work that is intended for him who has but a limited time for laboratory work. The tests given are accurate and reliable and give the essentials for making of diagnosis. In the fore part of the work is found an excellent outline for the taking of clinical histories. It is a handy volume and of value to those for whom it is written.

Miscellany

CONSTIPATION OF INFANTS

In the adjustment of diet to the particular requirements of the individual infant, constipation is often a prominent symptom that must be taken into account.

The baby that is habitually constipated is not likely to make the progressive gain that is desired, and when this condition exists for any great length of time it may lead into serious digestive disturbances.

Efforts that have resulted in a large measure of success for the Mellin's Food Method of Milk Modification have brought to notice certain food changes which may be made use of in dietetic treatment of constipation. These food changes are briefly set forth in a pamphlet which physicians may obtain by writing to the Mellin's Food Company, Boston, Mass.

PROPAGANDA FOR REFORM

THE ACTION OF HEXAMETHYLEMIN.—It has been shown by Hanzlik and Collins that hexamethylenamin can act only in body fluids which are acid in reaction, namely the gastric juice and the urine. The only part of the body in which hexamethylenamin may be expected to exert an antiseptic action is in the urinary tract, and then only if the urine is acid. If the urine is not acid already sodium acid phosphate should be administered to render it so. The administration of sodium or potassium acetate or citrate, in sufficient quantity, will render an acid urine alkaline and inhibit the action of hexamethylenamin (Jour. A. M. A., Jan. 3, 1914, p. 43).

RADIUM IN CARCINOMA.—Sparmann reports on the after-history of fifty-three cases of carcinoma treated with radium. Of these eleven have died since the

treatment, in six the tumor has disappeared, in five the condition seems improved, in seven the condition is aggravated and in the others the treatment was not continued because the condition of the patients had become worse. While these results show that radium is a remedy of use in the treatment of cancer it is not a sovereign remedy as some enthusiastic reports would have use believe (Jour. A. M. A., Jan. 17, 1914, p. 212).

RADIUM SULPHATE.—Radium sulphate is supplied in the form of a mixture of radium sulphate and barium sulphate and is sold on the basis of its radium content. Radium Sulphate-Standard Chemical Co., Radium Chemical Co., Pittsburgh, Pa. (Jour. A. M. A., Jan. 3, 1914, p. 41).

THE QUALITY OF SODIUM ACID PHOSPHATE.—As it appears probable that the use of sodium acid phosphate will increase and since previous experience has emphasized the unreliability of little used drugs, the A. M. A. Chemical Laboratory deemed it important to examine the market supply. While the official sodium phosphate may be obtained of exceptional purity, the examination showed that the market supply of sodium acid phosphate was decidedly variable and much less pure, although not seriously impure. Based on the examination the laboratory proposed standards which were thought fair, both to those who make it and those who use it in their practice. The examination showed the product of the Mallinckrodt Chemical Works and of the Powers-Weightman-Rosengarten Company to comply with the proposed standards. Acting on the report of the laboratory, the Council on Pharmacy and Chemistry decided to describe sodium acid phosphate in New and Nonofficial Remedies and, having adopted the proposed standards of purity, accepted the two brands named for inclusion with N. N. R. (Jour. A. M. A., Jan. 10, 1914, p. 142).

WHEN IS A PATENT MEDICINE.—While some physicians and especially some medical journals have trouble in classifying certain proprietary medicines drug departments in department stores find the problem a simple one. In recent Chicago newspapers advertisements for Fellow's Syrup of Hypophosphites, Glycothymoline and Sal Hepatica look perfectly at home with Peruna, Circus Liniment and Beecham's Pills (Jour. A. M. A., Feb. 21, 1914, p. 631).

EFFECT OF TARTRATES.—Many of the organic acids, such as citric and acetic, are burned up in the body, giving rise to carbon dioxide and water; thus sodium citrate, for instance, acts just like sodium carbonate in the organism. On the other hand tartaric acid and its salts are for the most part not destroyed in the body and leave it in their original form and animal experiments have shown that large doses of tar-

trates may give rise to symptoms of nephritis. However, while the claim made for a certain baking powder that the tartaric acid of cream of tartar in it is "wholesome" is evidently unwarranted, W. Post has shown that in the doses in which tartrates in the form of purgative mixtures, etc. is ordinarily given, are probably without harmful effects (*Jour. A.M.A.*, Feb. 21, 1914, p. 616).

The Truth About Medicines

PYO-ATOXIN.—A box of Pyo-atoxin was submitted to the A.M.A. Chemical Laboratory for examination. The box contained thirty black capsules having the appearance of some of the popular gonorrhea nostrums. While the synonym "Pheno-Methylene-Formate" suggested that Pyo-atoxin was a definite chemical substance, the examination indicated that the powder contained in the capsules was a mixture of hexamethylenamin and methylene blue—two well known drugs the value and limitations of which are known to the medical profession. Pyo-atoxin is sold by H. O. Hurley, Louisville, Ky. and is said to be "An Antitoxic Agent Indicated in Gonorrhea, Cystitis Pyelitis and Bacteriuric Conditions" (*Jour. A.M.A.*, Feb. 14, 1914, p. 552).

LUCILE KIMBALL OBESITY CURE.—Lucile Kimball of Chicago comes to the obese with the message "I can make your fat vanish by the gallon." All that is needed, she says, is to take her treatment—no dieting, exercise or drugs needed. The treatment consists of pink pills, which are reported to contain red pepper, menthol and bitters, probably gentian or quassia; brown tablets which the chemists declared to be an old fashioned cathartic pill, and a powder, reported to consist of soap, Epsom salt and washing soda (*Jour. A.M.A.*, Feb. 21, 1914, p. 631).

LOUISEBAD REDUCTION SALT.—This is a white powder sold by Karl Landshut, Chicago, and is to be used dissolved in a bath. The A.M.A. Chemical Laboratory reported the powder to be composed of sodium sulphate, sodium chlorid and potassium chlorid. It is hardly necessary to say that taking a bath in a tubful of water in which a tablespoonful of the mixture has been dissolved would have no other effect than that obtained from bathing in the same amount of water without the mixture (*Jour. A.M.A.*, Feb. 21, 1914, p. 632).

EVERY WOMAN'S FLESH REDUCER.—This obesity treatment is sold by the Every Woman Company, Chicago, Ill. and is a white powder smelling strongly of camphor and is of the bath-powder type. Examination in the A.M.A. Chemical Laboratory indicated the powder to be a mixture of alum, Epsom salt with an effervescing base of citric acid and

sodium bicarbonate or possibly sodium carbonate with a small amount of camphor (*Jour. A.M.A.*, Feb. 28, 1914, p. 714).

"GET SLIM."—Jean Downs, New York, offers to reduce the obese with "a purely vegetable, pleasant, healthy drink." A box of "Get Slim" was examined in the A.M.A. Chemical Laboratory. It contained 15 large envelopes, the same number of smaller envelopes and a package of powder. The large envelopes appeared to contain only sugar tinted pink. The contents of the smaller envelopes appeared to be tartaric acid, also tinted pink. The white powder was concluded to be sodium bicarbonate only. The sugar and tartaric acid powders are to be made into lemonade with the addition of lemon. The bicarbonate of soda is dissolved and the solution taken before meals (*Jour. A.M.A.*, Feb. 28, 1914, p. 715).

PAM-ALA, ANOTHER WORTHLESS QUININ SUBSTITUTE.—According to advertisements Pam-ala, sold by the Pam-ala Company, New York, is "A new and efficient Remedy for Malaria." Its general characters, particularly its cumin-like smell, and also the advertising claims are very similar to Sinkina, a preparation which was shown to be worthless. Most of the testimonials sent out are rather old and are stated to come from physicians in Italy, Cuba, Porto Rico, Guatemala, etc. Two recent testimonials from physicians in the United States were investigated by the Council on Pharmacy and Chemistry and in each case it was found that the opinions had been based on insufficient trials and that the physicians on further use of Pam-ala had become convinced of its inefficiency. While the evidence indicated that the essential constituent of Pam-ala is oil of cumin, proven worthless in the investigation of Sinkina, a chemical analysis was not made by the Council because it was thought that the secrecy with which the identity of Pam-ala was surrounded and the extravagant and highly improbable claims were sufficient to condemn it (*Jour. A.M.A.*, Feb. 28, 1914, p. 715).

EXPURGO ANTI-DIABETES.—The claim made for Expurgo Anti-Diabetes (sold in Canada as Sanol Anti-Diabetes) that it is "The only positive cure for Diabetes" and others of this character should be sufficient to condemn it. Nevertheless medical journals advertise it and physicians have been found to give testimonials for it. Examination in the A. M. A. Chemical Laboratory showed that Expurgo-Anti-Diabetes is essentially a watery solution of plant extractives with small quantities of sodium salicylate and salt. The exploiters claim that their stuff contains the fruit and bark of jambul, rosemary, star anise and fluid extract of calamus, cinchona, cola, condurango and gentian. One of the claimed ingredients, jambul, was in vogue as a remedy for diabetes some years ago. It was tried and found wanting and relegated to the therapeutic scrap heap (*Jour. A. M. A.*, Jan. 24, 1914, p. 312).

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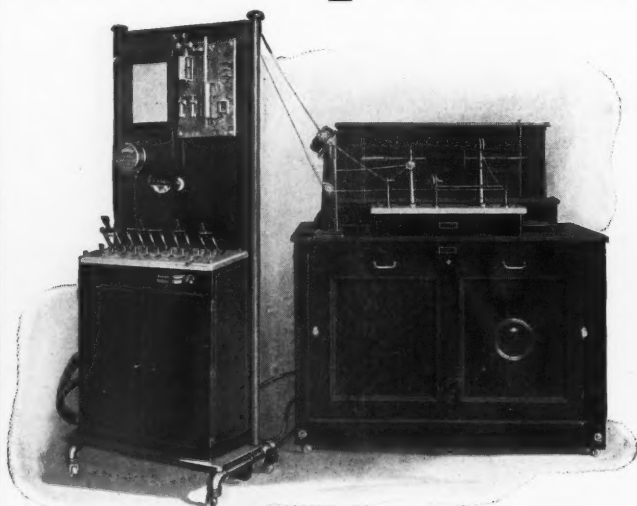
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